Placental blood transfusion in newborn babies reaches a plateau after 140 s: Further analysis of longitudinal survey of weight change

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Abstract

Objective: With the introduction of active management of the third stage of labour in the 1960s, it became usual practice to clamp and cut the umbilical cord immediately following birth. The timing of this cord clamping is controversial, as blood may beneficially be transferred to the baby if clamping of the cord is delayed slightly. There is no agreement, however, on how long the delay should be before clamping the cord. This study aimed to establish when blood ceased to flow in the umbilical cord to determine how long to delay clamping of the umbilical cord following delivery of the term newborn to maximise placental transfusion.

Methods: This observational study collected longitudinal weight measurements set in a hospital labour ward. A total of 26 mothers at term and their singleton babies participated in the study. In this reanalysis, the velocity of weight change over the first minutes of life determined by functional data analysis was estimated.

Results: We found that the flow velocity in the umbilical cord was on average 0 at 125 s after placing the baby on the scales, which was typically 140 s after birth.

Conclusions: To maximise placental transfusion, cord clamping should be delayed for at least 140 s following birth of the baby.

Keywords

Placental transfusion, labour, birth, neonate, functional data analysis

Introduction

Following birth of the baby, if the cord remains unclamped, blood continues to flow in the umbilical cord between the baby and placenta in both directions. The blood received by the baby during this time is known as placental transfusion. Immediate clamping of the umbilical cord following birth will potentially deprive the baby of the blood received from the placental transfusion that is potentially a valuable boost to the baby as a rich source of iron. A recent study supports this suggestion, reporting that clamping the cord at 3 min compared to clamping the cord before 10 s after birth led to improved iron stores at 4 months and reduced the prevalence of neonatal anaemia at 4 months following birth.¹ The increase in iron stores in the group with delayed clamping was attributed to the placental blood allowed to flow into the baby. However, a limitation identified was that it had not been possible to directly measure the amount of blood that actually transfused from the placenta to the newborn baby. This would have required an estimation of blood volume at the time of birth and following cord clamping. Although direct measurement of placental transfusion is arduous, it is not impossible, as we have recently demonstrated.²

Immediate clamping of the umbilical cord is an intervention associated with active management of the third stage of labour. There is clear evidence that the use of a prophylactic uterotonic³ and limited evidence that controlled cord traction⁴

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reduce the risk of haemorrhage; however, timing of cord clamping does not seem to influence this risk.⁵ There is no consensus regarding the best time to clamp the cord, because observational studies and randomised trials have either used different time delays for clamping or have neglected to report accurately the time of clamping all together. Also, evidence on important clinical outcomes is limited and long-term follow-up is minimal.^{5,6}

The duration and volume of placental transfusion seems to be influenced by position of the infant during the transfusion,⁷ mode of birth, either caesarean or vaginal delivery⁸ and administration of an intravenous ergot alkaloid.⁹ Ergot alkaloids are no longer used routinely, because of unpleasant side-effects. No recent trials have compared the effects of timing of oxytocic administration on placental transfusion. It is important to ascertain the time placental transfusion is complete to inform the intervention time for trials investigating the effects of timing of cord clamping. The aim was to determine when blood ceased to flow in the umbilical cord following birth and to determine how long to delay clamping of the umbilical cord following delivery of the term newborn in order to maximise the placental transfusion received.

Methods

Further details of recruitment and clinical procedures are given elsewhere.² Briefly, we recruited women at term with a singleton pregnancy who gave birth to a live baby at the Bradford Royal Infirmary, a hospital in the north of England. Mothers gave written consent and ethical approval was secured (Bradford Ethics Committee 08/H1302/65).

Procedure for weighing

As soon as practicably possible after delivery, the baby was placed onto digital scales (Mettler Toledo excellence XS precision balance Model: XS8001L) with the cord intact. The scales were zeroed to allow for the weight of a plastic sheet and 2 towels, used to wrap the baby. For vaginal births, the scale pan was either at the level of the introitus or the woman's abdomen. For caesarean births, it was either at the level of the bed or the woman's thighs. The clinician and the woman were informed of the need to place the baby on the scales as quickly as possible following birth and to refrain from touching the baby or the scales once weighing had started. The mean weight was measured every 2 s for up to 5 min following birth.

The cord was clamped if clinically indicated, if requested by the woman, or after 5 min, whichever arrived sooner. For all women, data were collected on timing of the uterotonic drug (oxytocin, intramuscular for vaginal births and intravenous for caesarean), time of cord clamping and position of the scale pan. For the baby, information was collected on time of birth (delivery of the buttocks for vaginal births, or the head for breech births). The attending midwife recorded the time when the baby was placed on the scales, times when the scales were knocked or disrupted and the time when the cord was readied for clamping. Clear deviations in weight were removed from the data.

Fitting a model to the weight data

Each weight measurement is not independent and will depend smoothly (in a mathematical sense) on the preceding weights: step changes in weight are not anticipated. We therefore model the weights as a trajectory, a continuous function of the weight measures that are collected every 2 s in time. Under these assumptions surrounding the form of the data, it is appropriate to use the mathematical technique of fitting 'splines' to the repeated measures.¹⁰ A polynomial function (for example, a cubic) is used as the basis of the spline to model weight against time individually for each baby.

The spline must satisfy certain conditions: it is constrained to pass though certain values of weight at specific times called knots, and at these knots, the spline function must be continuous (i.e. there are no breaks) and the function is smooth and there are no steps (mathematically, this means the velocity can be derived). The spline therefore constitutes a smooth function over the full range of the time data; hence, this approach is known as functional data analysis.¹¹ The number of knots required to ensure that the splines describe the data with sufficient fidelity was determined by fitting a generalised additive model, which uses generalised cross validation to determine the appropriate number of knots.¹² All statistical analyses were conducted in the statistical package R.¹³

Weight change

We are interested in the change in weight from the time at which the baby was placed on the scale to the time of clamping the cord. There is a short delay between birth of the baby to start of weighing, at which time the baby is being transferred to the scale. The start weight, at time zero, and end weights were estimated from the spline. The difference in weight, from birth to cord clamping, was calculated and 95% confidence intervals (CI) were used to determine the significance of the difference in start and end weights. In order to examine the dynamics of the change in weight, a Loess smoothed regression was fitted to the weight velocity (i.e. the first derivative against time).

The association between weight change and pre-specified sub-groups was examined: position of the baby and scales relative to the mother, oxytocin administration, vaginal or caesarean birth. These analyses were performed in Stata version 10.

Results

We recruited 28 mothers, but the weighing for 2 babies was truncated within seconds of delivery and these subjects were

Table I. Summary of weight, v	veight change an	d the tests of differen	ces between groups i	n
Time frame	n	Mean at	Mean at	

Time frame	n	Mean at start (g)	Mean at end (g)	Difference in means (g)	95% CI of difference (g)
Placed on scale to clamp	26	3295.0	3411.1	116.2	72.2 to 160.1
Placed on scale to 125 s	23	3190.0	3316.2	126.1	72.7 to 179.6
125 s to clamp	23	3316.2	3313.7	-2.5	-19.9 to 14.9
Clamp to end of weighing	8	3013.4	2994.5	-18.9	-47.4 to 9.6

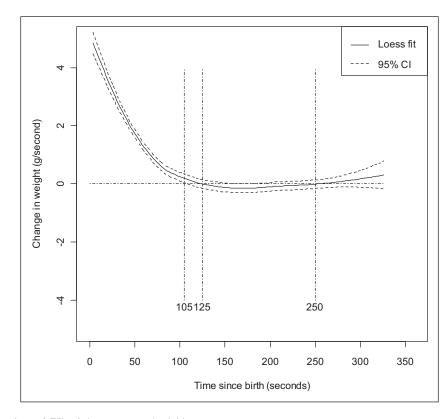


Figure 1. Loess curve (span 0.75) of change in weight (g/s) over time.

removed from the study. Table 1 summarises the mean weight; the mean start weight was 3295 g with a mean increase of 116.2 g in weight over the weighing period for the 26 babies. The 95% CI (72.2 to 160.1 g) shows that this is a significant weight gain. The weights of 8 babies were taken for a period of time following the clamping. This showed that blood transfusion has ceased, with a net weight loss of 18.9 g (95% CI: -47.4 to 9.6 g). From the birth of the baby to placement on the scale took 15 s (standard deviation (*SD*) = 13 s).

Figure 1 shows the change in the velocity of transfusion over the time of the weighing. The velocity is above 4 g/s for the first 10 s, and then the velocity decreases. The Loess curve suggested that placental transfusion intersects the zero line at 125 s, which represents the time when transfusion on average ceases.

After 246 s, the number of babies remaining on the scales dropped below 20, and it was decided that this was no longer

representative of the sample. Up until this point, from 105 s, the 95% CI suggests that the transfusion does not significantly change from zero. The weight change from birth to the point identified on Figure 1, at 125 s, was 126.1 g (95% CI 72.7 to 179.6 g); with no substantial weight change after 125 s up until the time the clamp was applied.

mean weight change.

Discussion

We have shown that placental blood transfusion plateaus at 125 s following placement of the baby on our scales. There is a typical delay of 15 s, however, from birth to the baby being placed on the scale, during which time blood flow in the umbilical vessels is likely to occur. Adjusting for this time delay, placental transfusion typically plateaus at 140 s following birth.

The time from delivery of the buttocks to baby being placed on the scales was variable and affected by factors

such as untangling baby from the cord, mode of delivery and the practitioner. Transfusion was only measurable when the baby was on the scales; therefore, it is likely that the volumes presented in this study are underestimations.

The key advantage of this technique is that the relatively intractable task of analysing a large number of data points distributed in time is replaced by the relatively simple task of extracting information from a single well-defined mathematical function. We used one very sensitive weighing instrument, and therefore, there should be minimal inter-baby weighing measurement error.

This is, we believe, the first study since the 1960s to address this issue, and we do so with a fairly direct method.⁸ There is renewed interest in the effect of timing of cord clamping and the effect of immediate or early cord clamping as a component of active management of the third stage. There is limited evidence to support any one timing of cord clamping over another as trial methodology differs and few trials have reported substantive outcomes for mother and baby or carried out long-term follow-up. The UK National Institute for Health and Care Excellence (NICE) guidelines¹⁴ for intrapartum care advise 'early clamping and cutting of the cord' as part of active management, though this guideline is now under review.

The position of the baby during the transfusion may affect the rate of umbilical blood flow, as the return from placenta to baby is partly gravity driven. Early studies suggest, however, that ensuring the baby is within 10–20 cm of the placenta will prevent the effect of gravity,⁷ and our more recent work supports this.² Women are encouraged to have skin-toskin contact with their babies as soon as possible after birth to facilitate bonding and breast feeding and prevent cooling of the baby. Our data suggest that holding the baby at the level of the abdomen will not affect the rate of placental transfusion in any substantive way.

All babies in this study were born at term. However, there appears to be the potential for a greater beneficial effect from delaying cord clamping and allowing placental transfusion in preterm infants,¹⁵ though data are few and the duration and volume of placental transfusion are unknown and should be explored to inform the intervention timing in trials investigating the effects of timing of cord clamping for this vulnerable group.

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Declaration of conflicting interests

G.R.L., B.C., D.F., E.M.S., and M.S.G. have no financial or non-financial interests that may be relevant to the submitted work.

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References

- Andersson O, Hellstrom-Westas L, Andersson D, et al. Effect of delayed versus early umbilical cord clamping on neonatal outcomes and iron status at 4 months: a randomised controlled trial. *BMJ* 2011; 343: d7157.
- 2. Farrar D, Airey R, Law GR, et al. Measuring placental transfusion for term births: weighing babies with cord intact. *BJOG* 2011; 118(1): 70–75.
- Cotter A, Ness A and Tolosa J. Prophylactic oxytocin for the third stage of labour. *Cochrane Database Syst Rev* 2001; 4: CD001808.
- Althabe F, Aleman A, Tomasso G, et al. A pilot randomized controlled trial of controlled cord traction to reduce postpartum blood loss. *Int J Gynaecol Obstet* 2009; 107(1): 4–7.
- McDonald SJ and Middleton P. Effect of timing of umbilical cord clamping of term infants on maternal and neonatal outcomes. *Cochrane Database Syst Rev* 2008; 2: CD004074.
- Hutton EK and Hassan ES. Late vs early clamping of the umbilical cord in full-term neonates: systematic review and meta-analysis of controlled trials. *JAMA* 2007; 297(11): 1241– 1252.
- Yao AC and Lind J. Effect of gravity on placental transfusion. Lancet 1969; 2(7619): 505–508.
- Yao AC, Wist A and Lind J. The blood volume of the newborn infant delivered by caesarean section. *Acta Paediatr Scand* 1967; 56(6): 585–592.
- Yao AC, Hirvensalo M and Lind J. Placental transfusion-rate and uterine contraction. *Lancet* 1968; 1(7539): 380–383.
- 10. Hastie T, Tibshirani R and Friedman J. *The elements of statistical learning*. 2nd ed. New York: Springer, 2009.
- Ramsay JO and Silverman BW. Functional data analysis. 2nd ed. New York: Springer, 2005.
- 12. Wood SN. *Generalized additive models*. London: Chapman & Hall, 2006.
- 13. R Development Core Team. *R: a language and environment for statistical computing*. Vienna: R Foundation for Statistical Computing, 2004.
- National Collaborating Centre for Women's and Children's Health. *Intrapartum care: care of healthy women and their babies during childbirth*. London: RCOG Press, 2007.
- Rabe H, Reynolds G and Diaz-Rossello J. A systematic review and meta-analysis of a brief delay in clamping the umbilical cord of preterm infants. *Neonatology* 2008; 93(2): 138–144.