

Brain injury at birth.

David J R Hutchon*

Emeritus Consultant Obstetrician , Memorial Hospital, Darlington. UK

Abstract

Brain injury at birth, most commonly caused by hypoxia and ischaemia lead to encephalopathy shortly after birth. The incidence has not changed in the last 40 years. The outcome in some neonates of permanent long-term brain injury remains a major problem in obstetrical and neonatal medicine. Despite significant changes in practice the incidence of cerebral palsy has not improved. We review the underlying pathology and highlight a possible cause which has been largely ignored until recently. Interfering with the transitional circulation by early cord clamping results in a 50% reduction in cardiac output and will exacerbate any ischaemic injury. For the infant who is already hypoxic, this could be critical. Solutions to a change in labour room practice to avoid this iatrogenic injury are provided.

Keywords: Brain injury, Hypoxia, Ischaemia, Encephalopathy.

Accepted on October 09, 2017

Introduction

What is known about the causes of hypoxic ischaemia during birth?

Electronic Fetal Monitoring: The clinical signs of hypoxia during birth have been recognised since the work of Hon over 50 years ago when he described the fetal heart rate response to hypoxia [1]. Fetal heart activity is the only measure of fetal health available continuously during labour, although fetal blood sampling is available intermittently to determine the degree of acidemia. Caesarean section can be used to deliver a baby suffering from intrapartum hypoxia and this is the rationale behind fetal heart monitoring to prevent brain injury and death during labour. Bradycardia is one of the responses of the heart to hypoxia and with fetal bradycardia the cardiac output falls. Since the fetal cardiac output is largely dependent upon heart rate, the cardiac output falls proportionately. Lower cardiac output will also lead to increasing ischaemia especially significant in the cerebral circulation.

Successful relief of intrapartum hypoxia by delivering the baby out of the uterus depends entirely upon effective transition and pulmonary respiration being established after birth. The respiratory centre is depressed by severe hypoxia with the neonate in a phase of primary apnoea. From animal studies it is thought that the asphyxiated neonate can recover its respiratory drive from primary apnoea spontaneously. However, if the intrapartum hypoxia continues long enough the neonate is delivered in secondary apnoea and recovery of the respiratory drive will not be possible. When a neonate is delivered and fails to breath it is not possible to know whether the neonate is in primary or secondary apnoea, so it is imperative the ventilatory help is given immediately.

Ideally with intrapartum monitoring the presence of hypoxia will be detected early enough to allow the delivery of the neonate before it has entered primary apnoea. The neonate will therefore be delivered in good condition and establish

respiration quickly. With effective pulmonary respiration after birth there will be no opportunity for further hypoxia and the hypoxia and acidemia will be quickly reversed allowing recovery of the heart rate and cardiac output.

Reperfusion brain injury

It is well recognised that more injury to the brain can occur during the reperfusion phase than during the episode of hypoxic ischaemia [2]. One strategy to minimise the injury is by hypothermia treatment or hypothermia treatment in combination with other neuroprotective agents [3,4]. It goes without saying that reperfusion injury will not occur if cerebral perfusion is maintained and does not fall below a critical threshold.

Failure of improvement with Electronic fetal monitoring

Since the introduction of the cardiotocograph (CTG) and other forms of Electronic Fetal Monitoring (EFM) over 40 years ago there has been an expectation that the effects of intrapartum hypoxia would fall. Disappointingly however there has been no fall in intrapartum deaths, neonatal deaths associated with hypoxia nor in cerebral palsy and other brain injury associated with hypoxia during labour. Further randomised controlled trials and systematic reviews have also failed to show a benefit of EFM although a reduction in neonatal fits was found when EFM was employed. This may represent a slight reduction in brain injury by the timely delivery of the hypoxic fetus.

Explanations for failure

Explanations for the failure of EFM have included poor interpretation of the CTG and faulty capture of fetal heart signal but attempts to remedy these weaknesses have, so far, not achieved better outcomes.

No matter how good the interpretation of the EFM signal to identify fetal hypoxia and no matter how timely the delivery of the fetus from the hypoxic environment of the uterus, if the hypoxic neonate is subjected to a 50% reduction in cardiac output followed by a significant interval before establishment of the functional residual capacity by ventilation, any ischaemic injury of the brain could be exacerbated [5]. This ischaemic injury of the brain will sometimes reach a critical threshold.

Cord Blood Gases

Cord blood gases are measured to provide a retrospective assessment of the degree of intrauterine hypoxia to which the fetus has been subjected. They are used as an audit tool for the quality of the care during labour and the results are also valuable evidence in medico-legal cases. Current practice recommends early cord clamping in order to measure cord blood gases. Cord blood can however be taken from the intact cord without clamping [6].

The relationship between umbilical cord arterial pH and serious adverse neonatal outcome is not as strong as might be expected and most neonates with neurological morbidity have normal cord pH values [7]. Impey et al. proposed that there may be a missing factor and agreed "it is indeed possible that neonatal hypovolaemia as a result of ECC could compound other factors, or be contributory in itself [8].

Cord Clamping

Early cord clamping after birth has now been removed from the active management of the third stage of labour to reduce the risk of post-partum haemorrhage by the National Institute of Clinical Excellence (NICE) and is also recommended in term neonates not requiring resuscitation by the International Liaison Committee on Resuscitation (ILCOR) [9,10]. There is no specific advice for the asphyxiated neonate who does require ventilation and further research is recommended but based on animal studies cord clamping before the onset of ventilation leads to a fall in cerebral perfusion and could exacerbate ischaemic injury of the brain [5]. There is additional support from our understanding of the physiology of transition [11]. In 1981 Peltonen recognised that "There is ... good reason in cases of resuscitation to keep the placental circulation intact" [12].

Current practice and recommendations

All current guidelines for the care of the neonate at birth include delayed cord clamping of at least one minute for uncompromised neonates. During that minute there must be the normal care for the infant such as drying, assessment and stimulation. There must be a suitable surface for the neonate to lie on and adopt a position which will permit the airway to remain open, with access for carers to provide drying and warming and for them to determine heart rate and breathing. This may not be a major problem for the normal birth, but it cannot be provided without preparation at a caesarean birth or an assisted vaginal birth. If babies are to receive the care and

assessment currently recommended preparation is essential at all births. The obstetrician or midwife who makes a snap decision as soon as the baby is born, without proper assessment, is not acceptable. However, if the preparation and facilities are in place to allow proper assessment of all babies with the cord intact immediately after birth, then there is nothing to prevent more intensive care such as ventilatory support to continue after the end of one minute. In other words, the ability to provide delayed cord clamping for all uncompromised babies requires a facility which can be used to provide delayed cord clamping and resuscitation for the majority of compromised babies.

Resuscitation with an intact cord at the mother's side

Early cord clamping facilitates the traditional practice of resuscitation of the neonate away from the mother on a standard resuscitation trolley at the side of the delivery room. If exacerbation of the hypoxic ischaemic insult is to be avoided in the asphyxiated neonate and delayed cord clamping, provided even in neonates requiring resuscitation, a significant change in delivery room practice and close collaboration between obstetric and neonatal staff will be required. These changes are already being developed and several approaches are possible [13-15].

Cord milking is another approach under consideration to reduce the hypovolaemia caused by early cord clamping. It might be argued that cord milking is not physiological and there is no evidence to show that it avoids an exacerbation of the hypoxic ischaemic insult.

Asphyxia during labour and assessment at birth

Asphyxia at birth cannot be reliably anticipated. In the absence of breathing the decision to initiate ventilation largely depends on the single parameter of heart rate. "In the first few minutes, the heart rate of an infant is usually judged best by listening with a stethoscope. It may also be felt by gently palpating the umbilical cord but a slow or absent rate at the base of the umbilical cord is not always indicative of a truly slow heart rate" [16]. The heart rate can only be judged by auscultation and there is no documentation or confirmation by a second attendant. The decision may often be influenced by the CTG and first impressions of the neonate. Although a minute is recommended before initiating aggressive resuscitation - to assess the condition, count the heart rate and dry the newborn baby - in practice decisions are made within seconds based on the CTG and first impressions [10]. Thus, the decision to initiate positive pressure ventilation before the end of the first minute is not consistent and is based on poorly documented criteria.

Neonatal bradycardia

Bradycardia occurs with early cord clamping especially if this is carried out before the onset of established breathing [17,18]. Therefore, the one-minute APGAR will be lowered simply as a result of early cord clamping. In normal birth weight infants, a low Apgar score is strongly associated with cerebral palsy [19].

Lie et al suggested that that the causes of cerebral palsy are closely linked to factors that reduce infant vitality [19]. Early cord clamping is known to reduce infant vitality. Early cord clamping is such a very common intervention at birth and until recently recommended as part of active management of the third stage of labour, it is clear that most infants must be able to compensate and tolerate the insult with little difficulty. However, a few cannot tolerate the hypoxia and hypovolaemia and their vitality is significantly reduced. Hypoxia may be corrected with timely ventilation but it may be some time before the hypovolaemia is recognised and corrected. During this interval there will be poor pulmonary blood flow and poor oxygenation in addition to hypoxic ischaemia in the cerebral circulation.

Conclusion

There can be no doubt that in a small number of neonate's early cord clamping causes or exacerbates hypoxic ischaemia of the cerebral circulation. This is one cause of brain injury during birth. Early cord clamping is an intervention which serves no purpose other than the rapid and convenient separation of the baby from its mother. The control of this intervention is entirely in the hands of the profession and if there was the will, the practice could be stopped within months by making the necessary changes in delivery room practice.

References

1. Hon EH, Reid BL, Hehre FW. The electronic evaluation of the fetal heart rate II. Changes with maternal hypotension. *Am J Obstet Gynecol.* 1960;79:209.
2. Peeters-Scholte C, Braun K, Koster J, et al. Effects of allopurinol and deferoxamine on reperfusion injury of the brain in newborn piglets after neonatal hypoxia-ischemia. *Pediatr Res.* 2003;54: 516–22.
3. Shankaran S. Outcomes of hypoxic-ischemic encephalopathy in neonates treated with hypothermia. *Clin Perinatol.* 2014;41:149-159.
4. Thoresen M, Hobbs CE, Wood T, et al. Cooling combined with immediate or delayed xenon inhalation provides equivalent long-term neuroprotection after neonatal hypoxia-ischemia. *J Cereb Blood Flow Metab.* 2009;29:707-14.
5. Martinello K, Hart AR, Yap S, et al. Management and investigation of neonatal encephalopathy: 2017 update. *Arch Dis Child Fetal Neonatal Ed.* 2017;102:F346–F358.
6. Wiberg N, Kallen K, Olofsson P. Delayed umbilical cord clamping at birth has effects on arterial and venous blood gases and lactate concentrations. *BJOG.* 2008;115:697–703.
7. Yeh P, Emary K, Impey L. The relationship between umbilical cord arterial pH and serious adverse neonatal outcome: analysis of 51 519 consecutive validated samples. *BJOG.* 2012;119:824–31.
8. Impey L. The missing peripartum deleterious process may be early cord clamping. Authors reply. *BJOG.* 2013;120:1030-1.
9. NICE guidelines [CG190] (2014) Intrapartum care for healthy women and babies.
10. Perlman JM, Wyllie J, Kattwinkel J, et al. Neonatal Resuscitation: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. *Circulation.* 2015;132(Suppl 1):S204-241.
11. Hutchon D, Bewley S, Nichol R. Support transition by keeping the placental circulation intact. *ADC Fetal and Neonatal.* 2008;93:5.
12. Peltonen T. Placental transfusion - advantage and disadvantage. *Eur J Pediatr.* 1981;137:141-6
13. van Rheenen PF. The role of delayed umbilical cord clamping to control infant anaemia in resource-poor settings. Amsterdam, The Netherlands: Rozenberg Publishers. 2007;p.130.
14. Hutchon D. Evolution of neonatal resuscitation with intact placental circulation. *Infant.* 2014;10:58–61.
15. Winter J, Kattwinkel J, Chisholm C, et al. Ventilation of Preterm Infants during Delayed Cord Clamping (VentFirst): A Pilot Study of Feasibility and Safety. *Am J Perinatol.* 2017;34:111-6
16. Wylie J, Ainsworth S, Tinnion R. UK Resuscitation Council. Resuscitation and support of transition of babies at birth. 2015.
17. Brady JP, James LS. Heart rate changes in the fetus and newborn infant during labor, delivery, and the immediate neonatal period. *Am J Obstet Gynecol.* 1962;84:1-12.
18. Hooper SB, Polglase GR, te Pas AB. A physiological approach to the timing of umbilical cord clamping at birth. *Arch Dis Child Fetal Neonatal Ed.* 2014;100:F1-F6.
19. Lie KK, Groholt E, Eskild A. Association of cerebral palsy with Apgar score in low and normal birthweight infants: population based cohort study. *BMJ.* 2010;341:c4990.

*Correspondence to

David J R Hutchon
Emeritus Consultant Obstetrician
Memorial Hospital
Darlington
UK