

NCT EVIDENCE BASED BRIEFING

Third Stage of Labour

Part 2: Active management of third stage

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This is the second of a two-part briefing on the third stage of labour. Part 1 covered the physiology of placental separation and how the baby adapts to life outside the womb, as well as physiological management of the third stage, including possible problems and ways of responding.¹

Part 2 includes:

- what is meant by the 'active management' of the third stage of labour, the usual method of managing the third stage in maternity units in the United Kingdom
- how active management affects the mother and baby, including both the advantages and disadvantages
- some of the other forms of management used in the third stage, including delayed active management and mixed management.

Introduction

Active management of the third stage involves a package of interventions aimed at preventing possible problems arising from placental separation and blood loss. It is a prophylactic, or preventative, approach. The generally accepted definition of active management is the combination of:

- a prophylactic uterotonic drug (a drug that makes the uterus contract), usually given with the birth of the baby's shoulder in the UK (though not in all countries)
- early cord clamping (ECC), usually immediately following the birth of the baby
- controlled cord traction (CCT), after awaiting signs of placental separation.²⁻⁴

The whole process, from administration of the uterotonic drug to the placenta emerging, normally takes about four to seven minutes.² Although the three essential elements are common, there are many variations in the way active management of third stage can be conducted⁴⁻⁶ as each component can be undertaken in a number of ways. It is important, therefore, when assessing research evidence to know the precise form of active management used, as this can make a significant difference to outcomes.

Variations in active management

Variations in the uterotonic drug used

A number of different prophylactic uterotonic drugs are used as part of active management to promote the separation of the placenta and reduce blood loss. In particular, the aim is to prevent postpartum haemorrhage (PPH) in those women who may be susceptible to it. Of the many possible uterotonic drugs to choose from, the first two listed here, oxytocin and Syntometrine, are most commonly used in the UK. The other drugs are included here as they have been used in research trials or are proposed as possible alternatives.

Oxytocin and its synthetic form syntocinon, can be given by intramuscular injection (IM), taking effect in about two minutes; or by intravenous infusion (IV) taking effect in about 45 seconds.⁷ There is some discussion around the optimum dose⁸⁻¹¹ and there are reported adverse effects on the mother's heartbeat and blood pressure with doses above 10 units.¹²

Syntometrine (a combination of syntocinon and ergometrine, sometimes referred to as Oxytocin-ergometrine), was developed in the 1960s for intramuscular use. It was thought that the combination of these two drugs gives a stronger more sustained contraction.^{7,11} Syntometrine is not recommended for women with raised blood pressure or with increased cardiovascular risk.^{13,14}

Ergometrine can be given by IM or orally, but the oral route appears to be no longer used because its effect is unpredictable.¹⁵ There is also no supportive evidence for the continued use of IV ergometrine due to adverse effects (e.g. increased risk of retained placenta, hypertension, headaches, dizziness, nausea, vomiting and reduced blood prolactin levels which might affect breastfeeding).^{2,7,16,17}

Prostaglandins (e.g. misoprostol) have been studied as a possible alternative choice as they can be administered orally and the drugs do not need to be stored under refrigeration – a considerable advantage in hot, low-income countries. Prostaglandins appear not to be as effective as other oxytocic drugs and have more adverse effects.¹⁸

Oxytocin antagonists are being considered but are not generally used in the UK.¹⁹

Choice of prophylactic uterotonic drug

Uterotonic drugs have been shown to reduce blood loss and haemorrhage at birth but to differing degrees and with differing adverse effects.^{9,11,15,18} Evidence comparing the effects of syntometrine and IM oxytocin suggests that for healthy women with no particular risk of haemorrhage, oxytocin could be a good choice if active management is to be used.^{11,20} These drugs have been compared in a systematic review which suggests that 10 units oxytocin IM show no significant difference in PPH (>1000ml) compared with syntometrine, with fewer adverse effects of raised blood pressure, nausea and vomiting.¹¹

Different times of administering the uterotonic drug

The prophylactic drug can be given with the crowning of the baby's head, with the birth of the baby's shoulder, after the birth but before the delivery of the placenta, or after delivery of the placenta.²¹ The timing of

administering the drug needs to be considered alongside the timing of clamping the cord, as the effects of these separate actions interact and their timing may make a difference to optimal outcomes.

The proposed advantage of giving the drug before the birth (as is generally done in the UK) is that it can begin to take effect sooner. However, this needs to be balanced against the possibility of delay in the baby being born, so the increased contractions may affect the baby and there may be an increased risk of retained placenta.²² Although undiagnosed twins are a rare problem these days, the second twin suffers badly if a uterotonic drug (e.g. IV ergometrine) is given after the birth of a first baby.²³

Different times of cord clamping

With active management the cord is normally clamped immediately after the birth of the baby, usually within 30 seconds, and before the cord had stopped pulsating.^{24,25} The earlier the cord is clamped the less blood will pass from the placenta into the baby by placental transfusion.^{24,26-31} Timing of cord clamping needs to be considered in relation to the timing and type of uterotonic drug used and decisions about cord traction.

Using placental cord drainage

After the cord has been clamped and cut, following early cord clamping, the placental end of the clamped cord can be released allowing free bleeding from the placenta. This makes the placenta smaller and more compact, and may make placental separation and delivery easier and with less blood loss.^{2,32}

Research evidence is scant but suggests that placental cord drainage may reduce the length of third stage, and the chance of a retained placenta, but showed no significant difference in the incidence of manual removal.^{32,33} Also, there is some evidence that placental cord drainage may reduce fetomaternal transfusion.^{2,34} Fetomaternal transfusion can occur when the placenta separates as there is a small risk that some of the baby's blood cells may get into the mother's circulation and stimulate antibody production (isoimmunisation).

Different ways of applying cord traction

Controlled cord traction was introduced with the aim of reducing blood loss by shortening the length of third stage, but it can be uncomfortable for the mother.^{7,35,36} It is now considered important that the uterus is well contracted before controlled cord traction is applied and a uterotonic drug should have been given.⁷ These protocols are not always adhered to in all the studies, and awaiting signs of separation has been the subject of some discussion.³⁷ Fundal pressure (putting manual pressure on the fundus when the uterus is contracted) has also previously been used to help deliver the placenta but appears to be no longer used in the UK.^{7,21,38-40}

Benefits and adverse effects of intervening routinely in third stage

Sometimes uterotonics are used therapeutically to stop excessive bleeding when it occurs, and sometimes they are used prophylactically, as part of active management, to reduce blood loss.^{3,41} There is widespread agreement

that therapeutic uterotonic drugs have made a major contribution to the reduction in maternal mortality and morbidity from postpartum haemorrhage. However, there remains controversy over the prophylactic intervention of active management, with some advocating that it should be used routinely for all women, and others believing that the balance of benefits and harms for low risk women support physiological management.^{3,7,42-44}

The International Confederation of Midwives (ICM) and the International Federation of Gynecologists and Obstetricians (FIGO) issued a joint statement supporting the use of active management but they define this as the administration of a uterotonic drug (IM oxytocin) within a minute of the birth of the baby, clamping the cord once pulsation ceases and applying controlled cord traction to deliver the placenta.⁴ So this is a different 'active management' from the standard one used in the UK.

It is important that the effects of all interventions are well understood, so that treatments are only offered to women if there is clear evidence that they do more good than harm, or offer valued opportunities for women and their families. Enkin et al. expressed this very clearly:

'We [have] worked from two basic principles: first, that the only justification for practices that restrict a woman's autonomy, her freedom of choice, and her access to her baby, would be clear evidence that these restricted practices do more good than harm; and second that any interference with the natural process of pregnancy and childbirth should also be shown to do more good than harm. We believe that the onus of proof rests on those who wish to advocate any intervention with either of these principles.'⁴⁵

Much of the evidence comparing planned active management with planned physiological third stage is reported in a systematic review.³ However, understanding the variations in the specific forms of active and physiological management used in the individual trials is important when considering the findings, because variations in the three components of active management may affect outcomes. For example, the inclusion in the review of a trial that used IV ergometrine as the prophylactic uterotonic drug is likely to overstate the benefits of reducing blood loss and haemorrhage because IV ergometrine is more effective than other drugs in this respect, but it has sufficient adverse effects in raising blood pressure that it is no longer used as part of active management of third stage in the UK.¹⁶

It is also important to understand the sample studied and methodology of each trial. The Hinchingsbooke trial studied low risk women only, whereas the Bristol trial included all women but then analysed a subset who were considered at low risk of haemorrhage.^{13,46} Subgroup analyses are less reliable if the randomisation is not stratified, because there is no assurance that underlying characteristics of the different treatment groups are similar. In addition, a significant number of women in the physiological arm of the two main trials in the review received 'mixed management'.^{13,46} Although this reflects what happened in the 'real world' in which the trials took place, with more experience of physiological management and different treatment protocols, outcomes for the physiological management arm of trials might be

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more favourable. The strengths and weaknesses of existing studies must be recognised when considering the evidence below.

Benefits and adverse effects of active management for the mother

Benefits

A systematic review of active versus physiological management of third stage in women at low risk of haemorrhage, by pooling data from three trials in a meta-analysis (Bristol [subgroup], Dublin, Hinchingsbrooke), shows beneficial differences in outcomes related to blood loss, anaemia and length of third stage with active management.³ However, the clinical significance of these findings is not clear cut, in part because the meta-analysis includes the Dublin third stage trial¹⁶ that used intravenous ergometrine, a drug no longer used as a prophylactic uteronic drug due to significant adverse effects.^{21,47}

Removing this trial from the meta-analysis leaves the results of a subgroup from the Bristol trial plus the Hinchingsbrooke trial being pooled.^{13,46} This data shows the following benefits of active management for the mother:

- reduction in the incidence of blood loss and haemorrhage, but the findings may not be clinically significant^{3,13,44,46}
- less chance of anaemia (haemoglobins less than 9g/dl) at one to two days after birth and need for a blood transfusion, but none of the studies assessed the effect of anaemia on women's tiredness, or how this affected their day-to-day lives^{48,49}
- a shorter third stage (the mean length was four minutes shorter, and fewer women had third stages lasting longer than 40 minutes).³

Adverse effects

These benefits need to be balanced against the possible harms. The systematic review and additional studies found a number of outcomes that were unfavourable with active management:^{2,3,7,50}

- more women had raised blood pressure after the birth (but this appears to be associated with the ergometrine component of syntometrine, and was not identified in the studies where IM oxytocin was used)¹¹
- more women had nausea and vomiting – this was particularly associated with the ergometrine component of syntometrine¹¹
- a larger, heavier placenta
- more chance of immunisation in Rhesus negative women^{2,51,52}
- two rare adverse events: snapping of the cord⁷ and inversion of the uterus.^{2,50}

There was no evidence in the systematic review of an increased risk of retained placenta with active management, as had been hypothesised, but variations in active management – with cord clamping being up to two minutes after birth in the Hinchingsbrooke trial, and the use of mixed management in both the Bristol and Hinchingsbrooke trials – may have affected this outcome.^{13,46}

Benefits and adverse effects of active management for the baby

Benefits

The systematic review shows no benefits for the baby from active management of the third stage.³ Apgar scores and admission to special care were similar when compared with physiological management.³

Adverse effects

However, there are five areas of additional risk for the baby that need to be considered.

1 **Blood loss and lower birth weight**

Clamping the cord immediately after birth interferes with the flow of blood from the placenta (placental transfusion), leaving the baby with around 30% less blood,^{24,28,30,31,53,54} and a lower birth weight.⁴⁶ Low blood volume has been suggested as an explanation for the failure of lung expansion observed in some babies, particularly premature babies.^{29,31}

2 **Breathing problems at birth**

Early cord clamping may contribute to breathing difficulties in some babies, particularly premature babies, or it may reduce a baby's ability to deal with breathing difficulties at birth.^{30,55-58} A baby who has difficulty in breathing at birth, and whose cord has been clamped, will need to rely on artificial oxygen ventilation as there is no further possibility of any placental oxygen supply. Although the placenta, in most cases, starts to separate fairly quickly after the birth of the baby, it has been suggested that this separation may be delayed and the cord pulsates for longer if the baby has difficulty in breathing.^{31,56,59}

Studies have been carried out on respiratory adaptation at birth in both full term and premature babies.^{27,28,57,58,60-62} For premature babies, the evidence is fairly clear: early cord clamping leads to more babies with low blood pressure, more babies needing a blood transfusion and more babies suffering from bleeding in the lungs (intraventricular haemorrhage).⁵⁷ For babies born at term, there has been little evidence collected from well designed trials on early cord clamping and the evidence is generally difficult to interpret due to methodological differences and poor reporting.^{25,63}

3 **Lower postnatal haemoglobin**

Immediate cord clamping results in a lower blood haemoglobin level for the baby compared to delayed clamping.^{2,24,30,54,64,65}

4 **Lower iron stores and anaemia at three to six months**

Iron stores at birth correlate with iron stores at six, nine and 12 months.⁶⁶⁻⁷⁰

5 **Rare adverse outcomes**

Undiagnosed additional babies, though very rare now in the UK, suffer a high rate of mortality (35%) and brain damage.^{23,71} Also, there is a hypothesised increased risk of cord stump infection, requiring investigation.⁷² These adverse effects mostly relate to the early cord clamping. The World Health

Organization (WHO) recommend delayed cord clamping as it may play a role in preventing iron deficiency anaemia and has no associated adverse effects.⁴³

Other forms of management of the third stage

Delayed active management

'Delayed active management' is the phrase used to describe the practice of administering a prophylactic uterotonic drug after the cord has finished pulsating and been clamped and cut, followed by controlled cord traction. This therefore:

- allows placental transfusion and so the baby receives its full amount of blood
- enables the placenta to reduce in size through placental transfusion
- gives more time for the placenta to be delivered before the uterotonic drug fully affects the uterus.

However, the mother is still at risk of increased blood pressure, nausea and vomiting from the uterotonic drug.

Whether delayed active management provides the proposed advantages of active management, i.e. reduced blood loss and reduced incidence of postpartum haemorrhage, has not been fully investigated.

Mixed management

'Mixed management' is the term used to describe care involving one or two components of active management (also sometimes called 'piecemeal approaches').² There is growing evidence that mixed management is unsatisfactory, leading to potential risks for both mother and baby. In 1989, Prendiville and colleagues called for further research on how best to intervene when physiological management was not proceeding normally:

'...there is a need to investigate whether it is preferable to resort to the full complement of active management (rather than a piecemeal approach) when there is need to interrupt the process of physiological management.'²

However, there has still not been any research specifically looking at this important question, and in the meantime mixed management has continued to be used – both in practice and in research studies.

The suggested disadvantages of mixed management are described below. Some are the same disadvantages as those associated with active management, others are exclusive to mixed management.

1 **Early cord clamping without prophylactic uterotonic drugs**

May increase blood loss, increase the length of third stage, increase the incidence of retained placenta and retained placental fragments.^{38,73}

2 **Controlled cord traction without a prophylactic uterotonic drug**

Very likely to increase blood loss and haemorrhage and is not recommended.⁷

3 **Prophylactic uterotonic without early cord clamping**

Causes a more rapid transfer of blood to the baby but appears not to alter the overall volume of blood transferred.^{24,29} Whether this more rapid transfer of blood causes some babies problems is unclear.

4 **Prophylactic uterotonic without controlled cord traction**

May increase the incidence of retained placenta. Oxytocic drugs can induce excessively strong uterine contractions and it is postulated that the cervix may close before the placenta is delivered if some form of cord traction is not used.³⁹

Although not conclusive, this evidence suggests that mixed management has disadvantages. While uncertainties will remain unless further research is carried out, it is suggested that these forms of third stage management are better not to be used outside an ethics-approved randomised controlled trial.⁴⁶

Therapeutic active management

The term 'therapeutic active management' is used to describe the therapeutic administration of the uterotonic drug, cord clamping and controlled cord traction. It may be used in situations where physiological management needs to be interrupted because of excessive blood loss, or the cord is tight around the baby's neck and cannot be released, although every effort should be made to allow placental transfusion first.³¹

Importance of the midwife's expertise

With active management of the third stage, low rates of PPH seem to be associated with labour attendants who are more patient and less inclined to intervene.⁷⁴ The Dublin third stage trial showed that it could take a considerable time for a midwife who is used to active management to become experienced in physiological third stage management.¹⁶ In this trial the PPH rate in the physiological management group showed a statistically significant decline ($p < 0.02$) as the trial progressed, being 12% in the first four months of the trial and 7% in the last eight months (having been 21% during the pilot study). In the Bristol third stage trial, 43% of midwives reported that they did not feel confident about physiological management at the beginning of the trial compared with just 2% after the trial.⁷⁵ In the Hinchingsbrooke third stage trial, there was slightly more blood loss over 500ml for women when the midwife was less confident with physiological management (14% compared with 11%) though the difference was not significant.⁴⁶

Active management of the third stage is routine practice in most British hospitals and not all midwives feel confident in physiological third stage management. It is important, therefore, for a woman wishing to have a physiological third stage to discuss this during pregnancy, preferably with the midwife who is to be with her in labour, to document her wishes in a birth plan and to discuss again with the midwife looking after her during labour.

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Summary

Essentially the third stage of labour can be managed in two ways. For healthy women, with an uncomplicated pregnancy and no history to indicate risk factors, who have had minimal interventions during the first and second stage of labour, a physiological third stage may seem the natural choice. The baby will benefit from a placental transfusion of about 30% additional blood. The evidence shows that there is more blood loss for the mother compared with active management, but the incidence of severe haemorrhage is low. The use of therapeutic uterotonic drugs is a very effective intervention if required.

For some women, the potential benefits of routine intervention with active management or switching to therapeutic active management if a planned physiological third stage is not straightforward, outweigh any potential harms of the uterotonic drugs, use of early cord clamping and controlled cord traction. Prophylactic intervention is of benefit where there is increased risk of haemorrhage in the mother, or when there have been interventions in labour which may interfere with the normal activity of the uterus during third stage. Delaying cord clamping provides benefits for the baby, and delaying active management may provide a better balance of benefits and harms for both mother and baby.

Key points

- Early cord clamping significantly reduces the passage of blood to the baby, which may interfere with the establishment of breathing in some babies, reduces birth weight and iron stores, contributing to anaemia. Conversely, delaying cord clamping significantly increases the baby's blood volume, may help if there are breathing difficulties at birth, increases birth weight and iron stores and reduces anaemia.
- Active management reduces blood loss and haemorrhage for the mother through the use of the uterotonic drug, but how much blood loss is normal for women after birth and at what level previously healthy women have adverse effects from moderate blood loss is unclear.
- Variations in active management may have different benefits and adverse effects. It is important to know the components of active management used in local maternity services, so women can make informed decisions about their care.
- More research is needed to address a number of remaining questions, including whether delaying the administration of the uterotonic drug until after the cord has stopped pulsating can provide benefits for the baby and the mother. The effects of blood loss for the women also need to be assessed.
- Further research is needed to explore optimal ways of intervening when the physiological approach is no longer appropriate.

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