

## POSTPARTUM HAEMORRHAGE (PPH) SYNTHESIS

Research Gaps from Cochrane Reviews (Cochrane Library Issue 1, 2008)

The faces indicate the direction of findings in each review:

- ☺ **Likely to be effective**
- ☹ **Both benefits and risks**
- ❓ **Uncertain or limited effect**
- ☹ **Likely to be ineffective or potentially harmful**

*Important research implications are more likely to arise from reviews with uncertain findings or where the benefits and risks are mixed*

### PRIMARY PPH

#### Prophylaxis

Pharmacological

Non-pharmacological

#### Treatment

Pharmacological

Non-pharmacological

### SECONDARY PPH

#### Prophylaxis

#### Treatment

### Primary PPH

#### Prophylaxis - pharmacological

##### ☺ **Active management in the third stage of labour (Prendiville 2000)**

- The individual components of active management (such as oxytocic administration, early cord clamping and cutting and controlled traction to deliver the placenta) warrant separate evaluation in RCTs.
- Need to explore effects of active management in differing clinical settings such as developing countries where the risk of maternal mortality associated with the third stage of labour is high.

##### ❓ **Oxytocin agonists for preventing postpartum haemorrhage (Su 2007)**

- Need large RCTs to determine whether carbetocin reduces PPH when compared with oxytocin.
- Need to determine the cost-effectiveness of carbetocin versus other uterotonic agents.

##### ☹ **Addition of ergometrine to oxytocin during the third stage of labour in order to prevent PPH (McDonald 2004)**

*Addition of ergometrine reduces risk of PPH (defined as blood loss of >500mls) but this has not been shown for severe PPH (>1000mls blood loss).*

*Ergometrine is associated with increased risk of nausea and vomiting and hypertension.*

- Further trials should assess whether higher doses of oxytocin have the same efficacy in preventing PPH as ergometrine without significant adverse effects

☺ **Prophylactic oxytocin in the third stage of labour to prevent PPH (Cotter 2001, McDonald 2004)**

- Need to determine optimal dosing and route of administration of oxytocin.
- Trials should address outcomes of immediate relevance to women in the postpartum period such as fatigue and the ability to care for their babies.

? **Timing of prophylactic oxytocics for the third stage of labour after vaginal birth (Soltani 2006)**

*Cochrane protocol, Cochrane review in progress*

? **Prophylactic ergot alkaloids in the third stage of labour to prevent PPH (Liabsuetrakul 2007)**

- Need to assess effect amongst women at increased risk of PPH
- Need to determine optimal dose and route of administration
- Need to assess maternal adverse effects
- Need studies from developing/resource-poor countries
- Need to assess neonatal outcomes and serious morbidity in the mother from PPH and possible adverse effects of ergometrine on lactation.

? **Prostaglandins for prevention of PPH (Gülmezoglu 2007)**

*There is evidence that misoprostol is effective for the prevention of PPH in out-of-hospital settings compared with placebo.*

- Need further studies of misoprostol in resource poor settings without access to medical professionals.
- Need to determine lowest effective dose and optimal route of administration for misoprostol.
- Intramuscular prostaglandins should be investigated only in high risk individuals due to their costs and side effects.

## **Prophylaxis – non-pharmacological**

? **Fundal pressure versus controlled cord traction as part of the active management of the third stage of labour (Peña-Martí 2007)**

*As there are no RCTs to support the use of fundal pressure rather than controlled cord traction as part of the active management of the third stage of labour, controlled cord traction is likely to continue as the method of placental delivery in the active management of third stage of labour.*

- Further trials comparing fundal pressure with controlled cord traction are probably not a research priority, as fundal pressure has been noted to have some disadvantages.

? **Early versus delayed umbilical cord clamping in preterm infants for preventing PPH (Rabe 2004)**

- Need maternal data from RCTs – none of the included trials reported maternal outcomes (several trials have recently been published and several more trials are still ongoing)

☺ **Delayed umbilical cord clamping of term infants on maternal and neonatal outcomes (McDonald 2008)**

- Need studies of adequate power and rigour to be able to detect the true advantages and disadvantages of cord clamping.
- Need to compare maternal outcomes such as PPH, longer term (6-12 months) postpartum follow-up on iron status, physical and psychological health, as well as short and longer term neonatal and infant outcomes such as neurodevelopment.

? **Manual removal of placenta versus cord traction at caesarean section for limiting maternal blood loss (Anorlu 2004)**

*Cochrane protocol, Cochrane review in progress.*

? **Placental cord drainage during the third stage of labour (with or without the prophylactic use of oxytocics) for the prevention of PPH (Soltani 2005)**

*There appears to be some potential benefit in the use of placental cord drainage in terms of reducing the length of the third stage of labour.*

- Need further large-scale RCTs to determine impact of cord drainage on the management of the third stage of labour and to assess neonatal outcomes.

? **Uterine massage for preventing postpartum haemorrhage (Hofmeyr 2007)**

*Cochrane protocol, Cochrane review in progress.*

## **Treatment - pharmacological**

? **Oxytocin agonists for treating postpartum haemorrhage (Su 2007)**

- Need to determine effectiveness of carbetocin as a therapeutic agent for PPH compared with other uterotonic agents.

? **Umbilical vein injection for management of retained placenta (Carroli 2001)**

*Umbilical vein injection of saline solution plus oxytocin appears to be effective in the management of retained placenta.*

- Need further adequately powered trials to assess effects of umbilical vein injection with oxytocin, prostaglandins and plasma expander.

? **Umbilical vein injection for the routine management of third stage of labour (Nardin 2006)**

*Cochrane protocol, Cochrane review in progress*

? **Pharmacological treatment for primary PPH (Mousa 2007)**

- Need multi-centre, double-blind, randomised controlled trials to identify the best drug combinations, route, and dose of uterotonics for treating primary PPH, that are large enough to assess maternal morbidity and mortality (several trials of misoprostol are ongoing)
- Need more trials of rectal misoprostol (one trial of misoprostol versus placebo in addition to routine treatment for PPH is ongoing)
- No trials of intrauterine misoprostol have been identified
- Need to follow agreed procedures for getting consent from critically ill patients and ensure that recruitment does not interfere with standard management
- Need to investigate interactions between misoprostol and other oxytocics
- Need trials to assess the effects of haemostatic drugs for treating unresponsive primary PPH (no trials identified)

## **Treatment – non-pharmacological**

### **[?] Surgical and radiological interventions for the treatment of primary PPH (Mousa 2007)**

- Need to follow agreed procedures for getting consent from critically ill patients and ensure that recruitment does not interfere with standard management
- Need trials to determine the best way of managing women who fail to respond to uterotonic therapy (no trials identified), such as interventional radiology
- Need to identify the most effective tamponade procedures and uterine haemostatic suturing techniques in women with major postpartum haemorrhage

## **Secondary PPH**

### **Treatment**

#### **[?] Drug versus surgical treatment for secondary PPH (Alexander 2002)**

- Need RCTs of treatments for secondary PPH – no trials have been identified

## **References**

- Alexander J, Thomas P, Sanghera J. Treatments for secondary postpartum haemorrhage. *The Cochrane Database of Systematic Reviews* 2002, Issue 1
- Anorlu R, Maholwana B. Methods of delivering the placenta at caesarean section. (Protocol) *The Cochrane Database of Systematic Reviews* 2004, Issue 2.
- Carroli G, Bergel E. Umbilical vein injection for management of retained placenta. *Cochrane Database of Systematic Reviews* 2001, Issue 4.
- Cotter A, Ness A, Tolosa J. Prophylactic oxytocin for the third stage of labour. *The Cochrane Database of Systematic Reviews* 2001, Issue 4.
- Gülmezoglu AM, Forna F, Villar J, Hofmeyr GJ. Prostaglandins for prevention of postpartum haemorrhage. *The Cochrane Database of Systematic Reviews* 2007, Issue 3.
- Hofmeyr GJ, Abdel-Aleem H. Uterine massage for preventing postpartum haemorrhage. (Protocol) *Cochrane Database of Systematic Reviews* 2007, Issue 2.
- Liabsuetrakul T, Choobun T, Peeyananjarassri K, Islam QM. Prophylactic use of ergot alkaloids in the third stage of labour. *The Cochrane Database of Systematic Reviews* 2007, Issue 2.
- McDonald S, Abbott JM, Higgins SP. Prophylactic ergometrine-oxytocin versus oxytocin for the third stage of labour. *The Cochrane Database of Systematic Reviews* 2004, Issue 1.
- McDonald SJ, Middleton P. Effect of timing of umbilical cord clamping of term infants on maternal and neonatal outcomes. *The Cochrane Database of Systematic Reviews* 2008, Issue 2.
- Mousa HA, Alfircvic Z. Treatment for primary postpartum haemorrhage. *The Cochrane Database of Systematic Reviews* 2007, Issue 1.
- Nardin JM, Carroli G, Weeks AD, Mori R. Umbilical vein injection for the routine management of third stage of labour. (Protocol) *Cochrane Database of Systematic Reviews* 2006, Issue 4.
- Peña-Martí G, Comunián-Carrasco G. Fundal pressure versus controlled cord traction as part of the active management of the third stage of labour. *Cochrane Database of Systematic Reviews* 2007, Issue 4.
- Prendiville WJ, Elbourne D, McDonald S. Active versus expectant management in the third stage of labour. *The Cochrane Database of Systematic Reviews* 2000, Issue 3.
- Rabe H, Reynolds G, Diaz-Rossello J. Early versus delayed umbilical cord clamping in preterm infants. *The Cochrane Database of Systematic Reviews* 2004, Issue 4.
- Soltani H, Dickinson F, Symonds I. Placental cord drainage after spontaneous vaginal delivery as part of the management of the third stage of labour. *The Cochrane Database of Systematic Reviews* 2005, Issue 4.
- Soltani H, Dickinson F. Timing of prophylactic oxytocics for the third stage of labour after vaginal birth. (Protocol) *Cochrane Database of Systematic Reviews* 2006, Issue 4.
- Su LL, Chong YS, Chan ESY, Samuel M. Oxytocin agonists for preventing postpartum haemorrhage. *The Cochrane Database of Systematic Reviews* 2007, Issue 3.