The prevention and treatment of postpartum haemorrhage: what do we know, and where do we go to next?

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Postpartum haemorrhage (PPH) remains a major cause of maternal deaths worldwide, and is estimated to cause the death of a woman every 10 minutes. This review presents the latest clinical advice, including new evidence on controlled cord traction, misoprostol, and oxytocin. The controversy around the diagnosis of PPH, the limitations of universal prophylaxis, and novel ways to provide obstetric first aid are also presented. It ends with a call to develop high-quality front-line obstetric services that can deal rapidly with unexpected haemorrhages as well as minimising blood loss at critical times: major abruption, placenta praevia, and caesarean for prolonged labour.

Keywords Maternal mortality, misoprostol, oxytocin, postpartum haemorrhage.

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Introduction

Postpartum haemorrhage (PPH) remains the most common cause of maternal mortality worldwide.[1] It is responsible for around 30% of maternal deaths, equivalent to 86 000 deaths per year annually or ten deaths every hour. Globally, mortality from PPH has reduced markedly over time. In the UK, maternal death rates from haemorrhage (per 100 000 maternities) have been falling steadily for the last 150 years, from a high of 108 in 1847.[2] By 1926 the rate had fallen to 50, and it continued to fall to 11 in 1952, and to the current rate of 0.4.[3] This compares with current mortality rates from haemorrhage in sub-Saharan Africa of around 150.

Although mortality from PPH is falling, there is evidence that the rate of both retained placentas and PPH is actually increasing in Western settings.[4,5] This appears to be a real effect, not simply a result of ascertainment errors or improved detection. The underlying reasons are unclear but are thought to relate to increased rates of intervention.

The modern risks of facility PPH in low- and middle-income countries were shown in the recent large WHO multi-country survey. Of 275 000 births, 1.2% of women had a reported PPH and there was an overall PPH death rate of 38 per 100 000 births. Of those with a PPH, 18% had a severe maternal outcome and 3% died.[6]

It is thought that most PPHs result from an atonic uterus, where the loss of myometrial tone allows maternal blood flow to the placental bed (500 ml/minute during pregnancy) to continue unchecked. Other causes include retained placental tissue, tears of the uterus, cervix, or vagina, and clotting disorders (the '4Ts' mnemonic: tone, tissue, trauma, and thrombin). Antenatal risk factors for PPH include Asian ethnicity, obesity, previous PPH, multiple pregnancy, anaemia, large baby, placenta praevia, and age over 40 years. Intrapartum risk factors include induction of labour, prolonged labour, intrapartum pyrexia, placental abruption, episiotomy, operative vaginal delivery, retained placenta, and delivery by caesarean section.[7]

There are three broad areas in which the outcomes from PPH may be improved: prevention, treatment, and rescue (Figure 1). Prevention covers antenatal strategies, active management of the third stage of labour, and treatments for retained placenta. PPH treatment covers both medical and surgical treatment, and PPH rescue therapies include intravenous fluids and blood transfusion, coagulation correction, and supportive care, such as compression garments. Each will be considered in turn in this review.
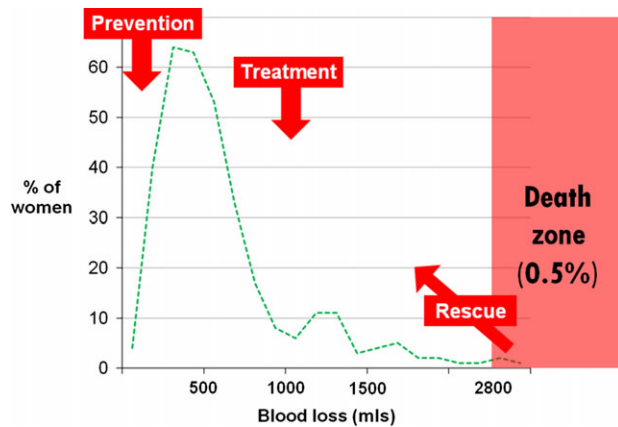
Figure 1. Histogram of blood loss at delivery showing the death zone at a loss of over 40% blood volume, and the three strategies for intervention. The data were adapted from Hoj,[58] with corrections to the published data. The Diagram is from Weeks.[59]

Preventing PPH

The long list of risk factors above shows how many factors in maternity care can affect the PPH rates. The association with anaemia is important because it appears to not only predispose women to PPH,[7] but also reduces tolerance to blood loss. The treatment of anaemia (both through the treatment of iron deficiency anaemia and through de-worming) is therefore important.

PPH is also closely related to surgical intervention, irrespective of whether this is induction, episiotomy, operative vaginal delivery, or caesarean section. Routine episiotomy is associated with a 27% increase in PPH at normal birth, and so should be used sparingly for delivery.[8] Reducing other surgical interventions is not so easy, but it should not be forgotten that PPH is one of the hidden costs of these interventions.

Active management of the third stage of labour

Active management of the third stage of labour was first described when purified oxytocin became widely available. Oxytocics were given to ensure effective uterine contractions, and the controlled cord traction (CCT) prevented retained placenta.[9] Early cord clamping was already commonly used and entered the protocol by default.[10] In 1988 the Bristol trial demonstrated that the 'active management' package reduced PPH rates,[11] and it rapidly became incorporated into standard labour management. The worldwide importance of PPH and the simplicity of the intervention meant that active management became 'a mantra for the safe motherhood movement'.[10]

There have now been seven major trials comparing an active management protocol with other packages, or normal management, that have found active management to consistently reduce excessive blood loss by 50–70%.[12] Many

of the studies in this review used combinations of oxytocin and ergometrine, and this was reflected in increases in hypertension and vomiting. There was no overall change in the need for the manual removal of placenta.

Recent studies have sought to examine the components of active management in more detail. Overall, they suggest that it is the oxytocic that is responsible for the beneficial effect of the package, with CCT contributing little, and early cord clamping having no maternal benefits, but introducing potential neonatal harm.[13] This is reflected in the latest WHO guidelines.[14] The studies that contributed to this finding are summarised below.

PPH medical prophylaxis

Oxytocin and carbetocin
Oxytocin is by far the most common prophylactic in use, and is usually given after delivery of the baby or the placenta.[15] This is also the drug recommended by the WHO,[14] the UK National Institute for Health and Care Excellence (NICE),[16] and the International Federation of Gynecology and Obstetrics (FIGO),[17] and is given as 10 iu intramuscularly at the time of delivery of the baby. Oxytocin can also be given as an intravenous bolus,[18] but causes a large, transient decrease in blood pressure when administered this way, and so should be administered slowly with care (Figure 2).[18] It had been thought that intramuscular and intravenous injections were equally effective, but a recent large randomised trial suggests that a low-dose intravenous infusion (10 iu over 1–2 hours) is more effective than 10 iu given intramuscular (I. Dzuba, pers. comm.);
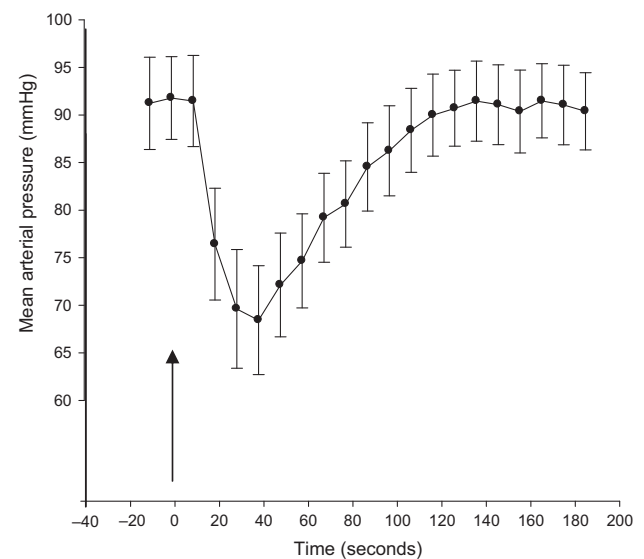

Figure 2. Effect of oxytocin bolus on maternal blood pressure (data from A. Carlin, pers. comm.). The arrow marks the time of oxytocin bolus. Diagram reproduced from Weeks.

however, there appears to be no benefit of using an infusion over 4 hours compared with a bolus over 5 minutes, at least in women undergoing caesarean section.[19]

Although oxytocin acts rapidly on the uterus (within a minute when given intravenously and within 2 minutes when given intramuscularly), the half-life of oxytocin is only around 10 minutes. A number of strategies have therefore been developed to prolong the oxytocic effect. These include combining oxytocin with the long-acting ergometrine, or the use of carbetocin, an oxytocin agonist. The clinical and pharmacological properties of carbetocin are similar to those of naturally occurring oxytocin, resulting in rhythmic contractions of the uterus within 2 minutes, and lasting 1–2 hours. There is evidence from randomised studies that carbetocin may be more effective than oxytocin,[20] and some countries have already adopted it as their first-line recommended oxytocic for PPH prevention at the time of caesarean section.[21] A heat-stable version of carbetocin has recently been developed, and a large WHO study is underway to test its efficacy in comparison with oxytocin.

Ergometrine and oxytocin/ergometrine (Syntometrine®)

Ergot derivatives were the first treatments described for PPH, with initial reports as far back as the end of the 19th century;[22] however, it was not until 1935 that the active substance was purified and named ergometrine.[23] Its administration causes an intense and sustained uterine contraction (in contrast to the intermittent contractions caused by oxytocin). A systematic review of its use for prophylaxis shows it to reduce the PPH rate (when used as part of the active management of the third stage of labour), compared with physiological management.[24] There are associated increases in hypertension, vomiting, and pain associated with its use, however, as well as an increase in retained placenta when it is administered intravenously.[25]

Ergometrine may be combined with oxytocin as a way of providing a sustained contraction after the oxytocin has worn off. The drug Syntometrine® has been commonly used in the UK,[15] and contains oxytocin 5 iu and ergometrine 500 µg. Systematic review shows Syntometrine® to be slightly more effective than oxytocin alone in preventing blood loss, but side effects are more common, with increased levels of hypertension, nausea, and vomiting.[26] The poor side effect profile has led to ergometrine being reserved for treatment rather than universal prophylaxis.

Misoprostol

The long shelf life and oral administration of misoprostol make it attractive for use in low-resource areas. It also has no effect on blood pressure or on the airways, and so can be safely used in women with asthma (in contrast to many of the prostaglandins, which cause broncho-constriction).

Its most common side effect is to offset the temperature regulation of the body. In those affected, the body attempts to raise its temperature by shivering. This can lead to temperatures of 40°C or more. Although these high fevers initially caused alarm,[27] experience has shown that they are self-limiting within 3 hours, and respond rapidly to tepid sponging and paracetamol.[28] The frequency of this side effect is related to dosage and route, with the highest rates of fever occurring with the sublingual route.[29] Genetic factors may account for the observed marked geographical differences in rates.

After many years of research into misoprostol for PPH prophylaxis, it appears that it reduces postpartum blood loss,[30] but that it is not as effective as oxytocin.[31,32] Oxytocin is therefore now recommended over misoprostol as a first line for PPH prophylaxis.[14,17] However misoprostol may be of benefit in settings with poor health services where there is limited provision of both refrigerators and skilled birth attendants. In these settings, misoprostol tablets can be given to women antenatally for self-administration at the time of delivery. Repeated studies have shown that this strategy is safe – women take the medication reliably and accurately (Weeks AD, Ditai J, Ononge S, Faragher B, Frye LJ, Durocher J, Mirembe FM, Byamugisha J, Winikoff B, Alfirevic Z, unpublished observations)[32] – and there are plans to disseminate this strategy widely.

The optimal dosage and route of prophylactic misoprostol is not known, but studies have used mainly oral or sublingual doses of 400 or 600 µg for prophylaxis. There is evidence that lower doses of misoprostol are as effective, but with lower side-effect rates,[28,34] and there have been calls for the use of reduced dosages;[35] however, both the WHO and the FIGO guidelines suggest the use of a single prophylactic dose of 600 µg of oral or sublingual misoprostol.[14,17]

Other third-stage components

Controlled cord traction

The role of CCT in maternal outcomes has recently been addressed in a large WHO trial where 24 390 women receiving oxytocin prophylaxis were randomised to either CCT or placental delivery by gravity and maternal effort alone.[36] There was no significant difference in the rate of severe PPH and there was only one uterine inversion (in the CCT group). Further analysis showed that CCT reduced the rate of retained placenta in those who had oxytocin/ergometrine prophylaxis, but had no effect if oxytocin was used alone. The results show that oxytocin can be safely used alone. Most practitioners will continue to teach and use CCT, however, as it may reduce minor PPHs, it shortens the length of the third stage, and it

prevents retained placenta when ergometrine is used as part of the third-stage package.[13]

Early cord clamping

Early cord clamping was one of the first routine interventions in labour, but systematic review shows that the timing of cord clamping has no effect on PPH rates or timing of placental delivery.[37] The placental transfusion (of 20–30% of the final neonatal blood volume) that results from deferred cord clamping, however, shifts the normal curve for neonatal haemoglobin to the right. This results in less neonatal anaemia but more hyperbilirubinaemia in the newborn. In settings where iron deficiency anaemia is common, therefore, early cord clamping is not recommended.[14,17] In Western settings early cord clamping has also largely been dropped because of concerns about the long-term effects of infant iron deficiency on neurological development.

Treatment of PPH

Medical treatment

Oxytocin

Despite being the first choice oxytocic for the management of atonic PPH, there are no randomised trials to demonstrate its efficacy against placebo. Evidence for its efficacy for PPH comes from trials on its prophylactic use, as outlined above. On the basis of this, the WHO recommends intravenous oxytocin for first-line management, with ergometrine (with or without oxytocin) or a prostaglandin drug (including misoprostol, 800 μg sublingually) as a second line.[14]

Misoprostol

Following years of small observational and underpowered randomised trials, three major trials were conducted into the use of misoprostol for PPH treatment. Widmer et al.[38] recruited 1400 women with PPH and compared the use of combined oxytocin and misoprostol (600 μg) with the use of oxytocin alone. The results show no difference between groups in additional loss of 500 ml (risk ratio, RR 1.01; 95% confidence interval, 95% CI 0.78–1.30) or 1000 ml (RR 0.76; 95% CI 0.43–1.34). The conclusion is that in settings where oxytocin is available for the treatment of PPH, there is no role for additional misoprostol.

The other two studies compared the efficacy of misoprostol and oxytocin as first-line treatments for PPH. The studies recruited a total of 40 000 women from a range of units throughout the world, some of which routinely gave oxytocin for prophylaxis,[39] and some that gave no prophylaxis.[40] The women who developed PPH were randomised to receive a high-dose oxytocin infusion (40 iu over 15 minutes) or misoprostol (800 μg, sublingually), each with placebos so as to ensure double blinding. In the units where there was no oxytocin prophylaxis there was less additional blood loss in those given oxytocin than for those given misoprostol. The difference was statistically significant for an extra loss of 300 ml (RR 1.78; 95% CI 1.40–2.26), but not for a loss of over 1000 ml (RR 1.67; 95% CI 0.40–6.96). In the units where women were given routine oxytocin prophylaxis, there was no difference in additional blood loss of 300 ml (RR 1.12; 95% CI 0.92–1.37), but more women in the misoprostol group had an additional loss of over 1000 ml (RR 3.61; 95% CI 1.02–12.85).

Together these three studies show that oxytocin is more effective than misoprostol for the treatment of PPH if it has not been previously given as prophylaxis, and that there is no benefit in giving misoprostol if oxytocin has already been used. For units that already stock oxytocin, therefore, there is little benefit in also stocking misoprostol.[41]

Tranexamic acid

This anti-fibrinolytic agent was first invented with a view to PPH treatment, but commercial interests led to it being finally developed for the treatment of menorrhagia. However, its use in PPH is being examined again and it is potentially attractive, given that it would reduce bleeding irrespective of whether it came from uterine atony or lacerations. Non-obstetric surgical studies have shown it to be effective in reducing blood loss, as have a few small obstetric trials.[42] A continuing large randomised study should clarify its role in PPH management (www.womantrial.lshtm.ac.uk).

Ergometrine

There is minimal evidence regarding the use of ergometrine for the treatment of PPH, although it is included in all the major PPH guidelines.[7,14,16,17] Its inclusion is justified on the basis of its demonstrated efficacy in the prophylaxis trials.

Physical treatments

There are several physical treatments for PPH available, but no randomised trials to evaluate their efficacy, except for the non-pneumatic anti-shock garment (NASG, see below). Observational studies of physical therapies generally show that bleeding stops rapidly, but this is not surprising given the natural history of PPH to improve spontaneously.

Non-surgical

The simplest of these treatments is uterine compression, usually achieved through bimanual compression with a fist in the vagina and hand on the abdominal wall. Although this appears to be highly effective, it is generally only used as a last resort as it is highly invasive and has overtones of gender-based violence. A less invasive option (the 'PPH

shelf') is currently being developed in Liverpool, UK (see below). An alternative is to compress the uterus by grasping it through the lax postpartum abdominal wall. Recent randomised trials suggest that this technique is beneficial for both prophylaxis and treatment of PPH.[43,44]

Aortic compression is also believed to be a highly effective way of reducing blood flow to the uterus, and thus treating PPH. Although uncomfortable, it can be maintained for over an hour when needed, and is a critical but underused intervention in severe PPH. It is especially useful for women with retained placentas who are bleeding heavily whilst they await the manual removal of the placenta.

Surgical

For PPH treatment at the time of caesarean or laparotomy, uterine compression sutures are now commonly used. The most popular is the B–Lynch suture, but this requires a lower segment caesarean section uterine incision. An alternative is the Hayman suture in which two front-to-back sutures are inserted the whole way through the uterine lower segment on the left and right side of the midline and each tied either side of the fundus.[45]

The alternative to compression with sutures is internal tamponade. This used to be achieved by packing with gauze, but balloon catheters are simpler to insert and remove, and minimise trauma to the decidua. The purpose-made Bakri balloon provides a central drainage channel and a 500–ml balloon capacity. A low-cost alternative can be made by tying a condom to the end of a large Foley catheter and holding it in place with a vaginal pack.[46]

Mass ligation, internal iliac artery ligation, and hysterectomy are surgical operations that require far greater skill. The mass ligation is the simplest and involves placing bilateral sutures into the uterus just above the level of the uterine artery. These horizontally positioned sutures pass front-to-back through the lateral part of the myometrium and return anteriorly through the broad ligament, thus enclosing the ascending uterine artery on both sides. This is often used as a low-risk first option before moving on to the more surgically complex internal iliac ligation or hysterectomy.

Rescue of women with severe PPH

Blood transfusion

The lack of donated blood for emergency transfusion is a major problem in low-resource settings: at least 26% of PPH deaths are thought to result from the lack of a blood transfusion.[47] Blood transfusion services are highly resource-intensive, and require voluntary donations, donor screening, and an effective, temperature-controlled distribution system. Despite their complexity, blood transfusion services are a crucial part of the health services required to prevent maternal deaths.

Recently it has become clear that specific clotting factors can be very helpful in both the diagnosis and treatment of PPH.[48] Fibrinogen levels fall early in women with PPH and appear to exacerbate the bleeding. The speed of the fall suggests that they are an important marker of the severity of the bleed, and the arrival of a bedside test (Rotem®, TEM Systems, Inc., Durham, NC, USA) means that the diagnosis can be made early. It also allows for rapid replacement, now also facilitated by the arrival of (the very expensive) freeze-dried fibrinogen concentrate. Initial studies suggest that it provides an important extra addition to the armoury in the fight against PPH deaths, at least for well-resourced settings.

Non-pneumatic anti-shock garment for transfer

The NASG was developed as a way of maintaining a soldier's blood pressure following traumatic injury during transfer from the battlefield to the hospital. The neoprene garment is wrapped tightly around the legs and abdomen, squeezing blood from the superficial vessels into the central vessels, and compressing the uterus. In animal studies the translocation of blood is up to 30% of the total blood volume.[49] The garment also reduces the available intravascular space, which in turn raises the blood pressure. The NASG offers considerable potential for use in low-resource settings as it is simple to apply, reusable, and relatively inexpensive ($160 per garment). Several observational studies have shown promise, and a major cluster randomised controlled trial (RCT) has recently been reported. The aim was to demonstrate a 50% reduction in 'extreme adverse outcome' by recruiting 2400 women in 24 clusters. Unfortunately, the study had to end prematurely because of a lack of funding after 880 women were recruited. There were no statistically significant improvements in outcomes, but the reduction in 'extreme adverse outcome' was 54% (odds ratio, OR 0.46; 95% CI 0.13–1.62), and the reduction in mortality was 46% (OR 0.54; 95% CI 0.14–2.05).[50] The WHO recommends its use as a temporising measure until appropriate care is available.[14]

Current issues in PPH care

Assessment based on blood-loss volumes

Postpartum haemorrhage (PPH) has been defined as the loss of over 500 ml of blood in the first 24 hours after delivery;[14] however, formal measurement of postnatal blood loss suggests that this volume of blood loss is very common, occurring in up to 50% of deliveries. In light of this, the Royal College of Obstetricians and Gynaecologists (RCOG) in the UK has amended its definition of PPH so that 500 ml is used as a point of 'alert', whereas treatment is

only given once the women has lost 1000 ml of blood.[7] All the above definitions suggest that an accurate knowledge of blood loss volume is important in the correct management of PPH. However, a major cluster RCT found that accurate measurement of blood loss using calibrated drapes did not reduce the total blood loss or improve outcomes.[51]

This has led to a reappraisal of the importance of blood loss volume assessment. It is likely that the assessment of blood loss volume has been given too much emphasis: practitioners do not base their decision to treat solely on repeated formal blood loss estimates, but more on a clinical decision based on a variety of factors, including background risk, rate of blood flow, practitioner personality, and availability of therapy, as well as the volume of blood lost. More research is required to understand this process, but a decision to treat based on the physiological response to blood loss, such as shock index (pulse/systolic blood pressure) or symptoms may be more appropriate.[52] A simple electronic monitor is being investigated that will rapidly diagnose shock and may prove a more effective diagnostic tool than blood volume assessment.[53]

How important are oxytocics in preventing deaths from PPH?

The arrival of misoprostol for PPH prevention and treatment generated great excitement because of the possibility of universal access to PPH prophylaxis, even amongst unattended home births. Although this has since been shown to be possible, the effect of this on maternal deaths is not known. There is evidence from several studies that the benefits of *prophylactic* oxytocics on blood losses of 500 and 1000 ml (and thus on postpartum anaemia) may not translate into reductions in PPH deaths. Furthermore, oxytocic *treatment* appears to only benefit a subgroup of women, especially if they have already had a prophylactic dose. For these reasons care must be taken to avoid an over-reliance on oxytocics and the neglect of other supportive and treatment measures. Three pieces of evidence support this view.

1 Historical data from the UK shows that the major reduction in PPH deaths occurred between 1850 and 1920, at a time when ergometrine was only sporadically available and in an impure format.[2] Much of the reduction in PPH deaths occurred before the arrival of purified oxytocics and the use of prophylaxis that started in the 1940s.
2 The natural history of PPH suggests that most atonic PPHs are self-limiting, and that atonic deaths are relatively rare. Although 10% of women have a PPH without prophylaxis, PPH deaths only occur in around 0.27% of women without access to health care (27% of deaths in low-resource settings are from PPH,[1] and the highest maternal mortality rates in the world are around 1000 per 100 000; this represents 270 per 100 000 or 0.27%). Of these deaths, most result from untreated pla-

centa praevia, retained placenta, or massive abruption. In South Africa, where access to oxytocics is not universal, the most common causes of PPH death are bleeding associated with caesarean section (26.2%), uterine rupture (17.9%), abruptio placentae (16%), and retained placenta (9.0%). Only 6% of PPH deaths result from uterine atony.[54]

3 In a recent secondary analysis of blood loss from two large studies in which blood loss was measured, statistical models were used to estimate blood loss in women who were not treated with oxytocics (Weeks AD, Lane S, Durocher J, Alfirevic Z, Winikoff B, unpublished observations). In women who did not receive oxytocin prophylaxis, most women stopped bleeding shortly after oxytocin or misoprostol therapy was given: around 30% more women than the 'natural history' predicted by the model. In those who had already received oxytocin prophylaxis, however, only 8% more women stopped bleeding than was predicted by the model.

There are many reasons why women with postpartum bleeds might have little response to oxytocics. Laboratory studies show that repeated exposure to oxytocin attenuates myometrial contractility,[55] and this will reduce the efficacy for those who have already received oxytocin prophylaxis. It may also reflect the fact that women with major PPHs are atypical, many have uterine abruptions, placenta praevia, pelvic infection, or retained placenta, and those whose uteri have not contracted in the normal way postnatally may not have uteri that respond well to oxytocin. All this points to a relative lack of efficacy of oxytocics for PPH treatment, and should warn practitioners about an over-reliance upon oxytocics when a woman is bleeding. It also suggests that there may be a benefit in using other therapies concurrently, rather than waiting for oxytocin to take effect.

Delivering PPH prophylaxis to women who have unattended home deliveries

Although it is uncertain how much benefit oxytocin prophylaxis can have in reducing maternal deaths, repeated studies have shown conclusively that it reduces PPH rates and postnatal anaemia. It is therefore an important intervention for preventing maternal morbidity; however, the provision of prophylaxis to those home births where there are no skilled attendants present has provided a challenge. Although misoprostol is not as effective as oxytocin, antenatal distribution for self-administration by the woman at the time of delivery has been shown to be safe (Weeks AD, Ditai J, Ononge S, Faragher B, Frye LJ, Durocher J, Mirembe FM, Byamugisha J, Winikoff B, Alfirevic Z, unpublished observations). The logistics of scaling this up remain a challenge, however, with issues concerning what to do with unused tablets, preventing the overuse of misoprostol

for labour induction, and providing effective antenatal education for its use. Inhaled oxytocin powder may provide an alternative, but may also have many of the same issues with its use.[56]

How best to deliver emergency care

In 2005 Hussein called for the development of 'obstetric first aid' skills and for its training in the community to be given as much priority as cardiopulmonary resuscitation.[57] Sadly, a decade later, little has progressed in achieving this aim and there is no agreed, coherent first-aid strategy for PPH. Part of this will be need to be an effective way to reduce blood loss rapidly, using aortic compression and/or bimanual compression. A less invasive option for uterine compression (the 'PPH Shelf') is currently being developed in Liverpool. This is based on the shelf pessary, used in gynaecological practice for treating uterine prolapse, and provides a platform against which the uterus can be compressed using a hand on the abdomen. Given that bleeding from the uterus should stop upon compression, whereas vaginal bleeding will persist, it may also prove to be a simple diagnostic tool. Human studies are in preparation to assess its efficacy and acceptability. The PPH shelf could prove to be a reuseable, simple method for both diagnosis and treatment, and could be an important tool for providing obstetric first aid. Further research is needed to optimise a first-aid package for community use.

Where do we go from here?

Despite huge investment in maternal health services throughout the world, PPH remains a major cause of maternal death. The rapid onset and progression of PPH means that high-quality services are required if we are to prevent PPH-related mortality and morbidity. The provision of uterotonics to all women is important, and the availability of misoprostol will help to reach women who do not otherwise have access to health services. But recent studies suggest that the main benefit of prophylaxis is a reduction in the rate of postpartum anaemia, with the effect on maternal deaths remaining less certain.

In women at low risk, around 3% will lose over 1000 ml of blood despite prophylaxis. These women require rapid access to life-saving PPH treatment and rescue therapies. However, the risk of major PPH is much higher in those with placental abruption, placenta praevia, obstructed labour, or multiple pregnancy, and these women are correspondingly less likely to respond to oxytocics. Large numbers of these women will require advanced PPH therapies or rescue treatments to prevent morbidity and mortality. The unpredictability of many PPHs means that skilled birth attendants will need to attend deliveries, have appropriate

obstetric first-aid skills and equipment, and the ability to transfer women rapidly.

If major improvements in PPH-related mortality are to be achieved, there will need to be an increased provision of high-quality emergency obstetric care services. This includes the provision of surgical services to prevent PPH (caesarean section and manual removal of placenta), PPH medical treatments (oxytocin and possibly tranexamic acid), physical treatments (uterine compression, balloon tamponade, and surgery), and rescue packages (blood transfusion and blood products). More research is now required to determine the most cost-effective way of providing these services.

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