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Prevention and Treatment of Postpartum Hemorrhage: New Advances for Low-Resource Settings

Suellen Miller, CNM, PhD, Felicia Lester, MPH, MS, and Paul Hensleigh, MD, PhD

Postpartum hemorrhage due to uterine atony is the primary direct cause of maternal mortality globally. Management strategies in developed countries involve crystalloid fluid replacement, blood transfusions, and surgery. These definitive therapies are often not accessible in developing countries. Long transports from home or primary health care facilities, a dearth of skilled providers, and lack of intravenous fluids and/or a safe blood supply often create long delays in instituting appropriate treatment. We review the evidence for active management of third-stage labor and for the use of specific uterotonics. New strategies to prevent and manage postpartum hemorrhage in developing countries, such as community-based use of misoprostol, oxytocin in the Uniject delivery system, the non-inflatable antishock garment to stabilize and resuscitate hypovolemic shock, and the balloon condom catheter to treat intractable uterine bleeding are reviewed. New directions for clinical and operations research are suggested. J Midwifery Womens Health 2004;49:283-292

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Vivio and Williams' recent commentary in this Journal[1] discussed the controversy among US-based midwives about the International Confederation of Midwives (ICM) and the International Federation of Gynaecologists and Obstetricians (FIGO) Joint Statement: Management of the Third Stage of Labor to Prevent Postpartum Haemorrhage.[2] As the authors stated, it is difficult to comprehend how postpartum hemorrhage can be the primary direct cause of maternal death, given the resources available to women who give birth in the United States. However, the situation in a resource-rich setting like the United States is far different from the resources available in the developing world, where most maternal mortality occurs. The lack of skilled attendants at delivery who can provide even the minimum of care, long transport times to facilities that can manage uterine atony or severe lacerations of the genital tract, and unattended obstructed labor leading to a ruptured uterus conspire to elevate postpartum hemorrhage to its position as the number one killer of women during childbirth. These structural factors are exacerbated by the prevalence of anemia, which is estimated to affect half of all pregnant women in the world, with that figure rising to 94% in Papua New Guinea, 88% in India, and 86% in Tanzania.[3] Anemia is rarely detected or treated during pregnancy and often exacerbated by malarial and other parasitic diseases.[4] Although the vast majority of cases of postpartum hemorrhage have no identifiable risk factor, young age at marriage[5,6] and low contraceptive use among many women in the developing world result in high total fertility rates, which results in more grand multiparas giving birth in low-resource countries compared with more developed countries.[7] Prevention of postpartum hemorrhage in developing countries is a critical goal.

In this article we discuss the problem of postpartum hemorrhage in the developing world and describe some of the newer technologies and strategies that are being developed for the management and treatment of postpartum hemorrhage in low-resource settings. We report on information from recent international meetings, such as the Bellagio meeting on reduction of maternal mortality,[8] the 2003 FIGO XVII World Conference of Gynecologists and Obstetricians, and the JHPIEGO/United States Agency for International Development-sponsored "Preventing Postpartum Hemorrhage: From Research to Practice" meeting in Bangkok, Thailand, January 2004.

ETIOLOGY OF POSTPARTUM HEMORRHAGE IN DEVELOPING COUNTRIES

A large percentage of births in the developing world occur at home without a skilled attendant present.[9] For example, 80% of women in rural West Africa deliver at home without skilled attendants[10] and more than 60% of births in sub-Saharan Africa and in South Asia occur without a skilled provider present.[6] Approximately 14 million women suffer from postpartum hemorrhage every year worldwide.[11] Without the presence of a skilled provider to recognize and treat the conditions leading to postpartum hemorrhage (uterine atony, uterine rupture, and/or genital lacerations) and to manage postpartum hemorrhage if it occurs, women rapidly experience shock and death, resulting in approximately 125,000 deaths per year due to primary postpartum hemorrhage.[12] Primary or early post-

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partum hemorrhage occurs in the first 24 hours after delivery, and uterine atony is the most common cause.[13] Lacerations of the vagina and cervix are another common cause of postpartum hemorrhage. In the United States, these lacerations occur more commonly with operative vaginal deliveries. In the developing world, they tend to happen when unskilled operators perform unnecessary forceps deliveries and when unskilled attendants allow or persuade women to push before the cervix is fully dilated. Toxemia and abruption of the placenta also contribute to postpartum hemorrhage through disseminated intravascular coagulopathy, as does, more infrequently, chorioamnionitis. Given the lack of access to facilities and providers, many women who are carrying an undetected retained dead fetus will likewise develop disseminated intravascular coagulation (DIC) with resultant uncontrollable hemorrhage. Inherited disorders of coagulation, which might have been identified in developed countries with the onset of menarche, often are not discovered until the woman develops severe postpartum hemorrhage in developing countries. Postoperative bleeding occurring during or after emergency or elective obstetric surgery can lead to postpartum death or morbidity. In addition to the etiologies of postpartum hemorrhage that occur in women with term pregnancies, there are also grave risks to women from ruptured ectopic pregnancies and postabortion hemorrhage, whether from unsafe abortion or from undiagnosed and unmanaged spontaneous abortions.

TREATMENTS FOR POSTPARTUM HEMORRHAGE IN LOW-RESOURCE SETTINGS

In more developed countries, management strategies involve crystalloid fluid replacement, blood transfusions, and surgery—definitive therapies best delivered in well-equipped and staffed facilities. In many primary care facilities there are no personnel trained to perform intravenous (IV) placement, even if IV fluids are available. Blood transfusion ability may be limited to the biggest city hospitals, and even there availability of safe blood is limited. Even the simplest therapies, such as fundal massage and intramuscular (IM) and/or IV oxytocin administration, are outside the training and skills of many birth attendants, if a birth attendant is present.

Health care providers involved in the Safe Motherhood Initiative,[9] ICM, FIGO, and other organizations devoted to making birth safer for women in all countries are looking to new strategies, techniques, technologies, and adaptations of underused technologies to reduce maternal mortality attributable to postpartum hemorrhage. As reported recently in the *Lancet*, there are several promising technologies for treatment of postpartum hemorrhage that are relatively simple, which can be used by personnel with limited skills and training and can be available in remote and/or rural areas of less developed countries.[8] These include 1) universal use of active management of third-stage labor, 2) oxytocin in Uniject (BD Pharmaceutical Systems) as a way of overcoming some of the barriers to oxytocin use in low-resource settings, 3) the use of oral and/or rectal misoprostol for prevention and treatment of postpartum hemorrhage, 4) the non-inflatable antishock garment (NI-ASG) for stabilization and resuscitation of hypovolemic shock secondary to postpartum hemorrhage, and 4) the hydrostatic condom balloon catheter to control intractable postpartum hemorrhage secondary to uterine atony.

ACTIVE MANAGEMENT OF THE THIRD STAGE OF LABOR

Expectant (also known as conservative or physiologic) management of labor involves waiting for signs of placental separation and allowing for spontaneous delivery of the placenta aided by gravity and/or nipple stimulation.[14] Active management of the third stage of labor was defined in the recent ICM/FIGO joint statement[2] as the administration of uterotonic agents, controlled cord traction, and uterine massage. Earlier definitions recommended an additional component of early clamping and cutting of the cord (before pulsation stopped). The newer ICM/FIGO definition reflects the evidence[15] that delayed cord clamping is actually beneficial, and early clamping and cutting of the cord has been deleted from the official definition of active management. As previously documented by Brucker,[16] strong evidence exists that active management prevents postpartum hemorrhage compared with expectant management. Studies have been conducted in low-resource settings to test this evidence in the parts of the world where women die in large numbers from postpartum hemorrhage.

A retrospective study from Ghana compared active versus expectant management in a rural setting at Holy Family Hospital in Berekum.[17] They performed a chart review of 5,088 birth records from women who delivered between 1992 and 1995 when expectant management was routine, compared with 3,840 records from women who delivered from 1996 to 1998 after the introduction of active management as the standard of care. The study found that postpartum hemorrhage (blood loss $\geq$500 mL) occurred less often in the actively managed group (odds ratio, 0.8; 95% confidence interval [CI], 0.7–0.9). This study yields a

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number needed to treat of 27, which means that 27 women would have to be actively managed to avoid one case of postpartum hemorrhage. They recommended active management as a strategy to reduce postpartum hemorrhage in rural hospitals in developing countries.[17]

McCormick et al.[18] published a systematic review of studies that assessed the efficacy of active management of the third stage in low-resource settings. Active management reduced the incidence of postpartum hemorrhage, decreased the need for blood transfusion, reduced the incidence of prolonged third stage of labor (>30 minutes), and decreased the need for additional uterotonic drugs. These authors found no difference between the groups in terms of increased blood pressure or manual removal of the placenta, and the incidence of retained placenta, uterine inversion, or cord avulsion was not increased in the actively managed group. The study concluded that active management of the third stage of labor should be expanded to developing countries as an effective, inexpensive intervention to prevent postpartum hemorrhage.

A 2003 Cochrane Review of active versus expectant management of the third stage of labor[19] included five randomized controlled trials (RCTs) and found that for all women, including women deemed to be at low risk for postpartum hemorrhage, active management decreased the incidence of postpartum hemorrhage (both 500–1000 mL and >1000 mL), shortened the third stage of labor, decreased the amount of maternal blood loss, decreased the need for blood transfusion, and decreased the need for additional therapeutic uterotonic agents. The incidence of postpartum hemorrhage 500 mL or more was reduced in the actively managed group (relative risk [RR], 0.38; 95% CI, 0.32–0.46). These figures translate to a number needed to treat of approximately 12, which means that for every 12 women who are actively managed rather than expectantly managed, one case of postpartum hemorrhage (defined as blood loss ≥500 mL) will be averted, whereas the number needed to treat for averting blood loss greater than 1000 mL would be 57 (calculation of NNT: 1/ARR where ARR = proportion of controls with postpartum hemorrhage minus the proportion of treatment group with postpartum hemorrhage: 1/[(428/3158) − (163/3126)] = 11. Women who were actively managed lost less blood with a weighted mean blood loss of 79.33 mL (95% CI, −94.29 to −64.37) less than those who were expectantly managed. The third stage was an estimated 9.77 minutes shorter (95% CI, −10.00 to −9.53) in actively managed women. In this review, actively managed women experienced nausea at a greater rate than expectantly managed women (RR, 1.83; 95% CI, 1.51–2.23), as well as vomiting and high blood pressure. The higher blood pressure was likely due to use of ergometrine in some studies.

The implementation of active management of third-stage labor remains controversial, despite the evidence of its efficacy in randomized trials.[1] The issue of active management of third-stage labor is further clouded by the lack of consensus on what the order of the actual steps are: uterotonic, plus controlled cord traction, plus fundal massage,[2] or uterotonic, plus early cord clamping, and controlled cord traction?[14] In addition, there is a variation of opinion of which uterotonic is most appropriate for low-resource centers and which route (parenteral, oral, or rectal) is to be used.

Despite lack of clarity on exactly how active management of third-stage labor should be performed, the ICM and the FIGO, representing midwives and obstetric specialist physicians from around the world, released their Joint Statement on the Management of the Third Stage of Labor to Prevent Postpartum Hemorrhage in November 2003.[2] Based on an extensive review of the literature, this document recommends that active management of third-stage labor be offered to *all* women, because 1) the presence of risk factors cannot be used to predict postpartum hemorrhage and 2) active management has proved to reduce the incidence of postpartum hemorrhage, the quantity of blood loss, and the use of blood transfusions.[19]

UTEROTONICS FOR PREVENTION OF POSTPARTUM HEMORRHAGE

The use of routine uterotonic agents to prevent postpartum hemorrhage can reduce maternal mortality by 40%.[20] For centuries, the uterotonic agent of choice has been oxytocin with or without supplemental ergot preparations such as ergometrine or methergine; both oxytocin and methergine are unstable at room temperature and thus require special temperature and light storage conditions to remain effective.[21] Moreover, such preparations must be administered intramuscularly. In many settings, lack of trained personnel and of refrigeration to store oxytocic agents undermines the potential for implementing the active management of third-stage labor.[21] Misoprostol, an oral preparation of prostaglandin (PGE_1) analogue, is a prime candidate given its uterotonic properties; ease of use as an oral, vaginal, or rectal preparation; relative low cost in some areas; and stability at high temperature.[22]

Several RCTs have been conducted to examine whether misoprostol is a suitable alternative to oxytocin in low-resource settings for prevention of postpartum hemorrhage. The World Health Organization (WHO) multicenter randomized controlled trial is, to date, the definitive equivalence study of oxytocin versus misoprostol.[23] The trial included 18,520 women from nine countries and compared 600 mg of misoprostol given orally with 10 IU of oxytocin given intramuscularly or intravenously. Misoprostol was not as effective at preventing postpartum hemorrhage (>1000 mL of blood) as was oxytocin.[21] The incidence of postpartum hemorrhage in those managed with misoprostol was 4% compared to 3% in those managed with oxytocin (RR, 1.39; 95% CI, 1.19–1.63). There was also a greater need for additional uterotonics in the misoprostol group than in the oxytocin group (15% and 11%, respectively

[RR, 1.40; 95% CI, 1.29–1.51; $P < .0001$]). Although statistically significant, these differences did not correlate with clinical outcomes, such as need for blood transfusion. In fact, fewer women given misoprostol needed blood transfusion than did women given oxytocin, but this difference did not reach statistical significance (RR, 0.74; 95% CI, 0.55–1.01, $P = .06$). Those given misoprostol were found to have a significantly higher rate of transient shivering and pyrexia than those given oxytocin, but no long-term harm was documented as a result of these side effects.

This study has been criticized in published commentaries.[24–27] Some argued that, given the vast heterogeneity between the nine study sites, the study should be considered a meta-analysis rather than an RCT.[26] On the basis of the problems with this large, influential RCT, many researchers and practitioners argue that there is "still room for discussion" of the role for misoprostol in the active management of third-stage labor[27] in low-resource settings.

Several smaller RCTs of misoprostol have been conducted in developing countries. An RCT in Mozambique found that rectal misoprostol (400 mg as rectal enema) was as effective as 10 IU oxytocin given IM in preventing postpartum hemorrhage.[28] Blood loss, duration of third stage, or hemoglobin and hematocrit at 72 hours postpartum were not significantly different between the groups. However, those who received misoprostol did have significantly higher rates of shivering and pyrexia. In a similar study in Zimbabwe, there was no significant difference in postpartum hemorrhage (loss of >500 mL blood, loss of >1000 mL blood, or need for additional oxytocic agents between women given 400 mg of oral misoprostol compared with those given IM 10 U of oxytocin). Again, misoprostol was associated with a higher incidence of pyrexia and shivering with no adverse clinical correlation.[21] A multicenter RCT from Hong Kong found no significant differences in the incidence of postpartum hemorrhage between the group receiving oral misoprostol and those who received IM syntometrine.[29] An RCT from Turkey found that oral misoprostol was as effective as oxytocin alone in preventing postpartum hemorrhage, but not as effective as oxytocin plus methylergonovine maleate or oxytocin plus oral misoprostol.[30] A review of misoprostol use during the third stage of labor, compared with both placebo and oxytocin or syntometrine, found that misoprostol is better than placebo in reducing the need for additional oxytonics but inferior to oxytocin in preventing postpartum hemorrhage, and it requires more additional use of oxytonics than syntometrine.[31]

A Cochrane Review meta-analysis[32] and a WHO systematic review[33] analyzed the data from various studies of misoprostol versus placebo and misoprostol versus oxytocin for prevention of postpartum hemorrhage. In both analyses, the misoprostol versus oxytocin arm was largely influenced by the WHO trial discussed above. The Cochrane review of misoprostol versus oxytocin included 24,100 women and compared various oral and rectal doses of misoprostol with injectable oxytocin. They found that 600 mg of misoprostol was less effective than oxytocin in preventing postpartum hemorrhage greater than 1000 mL (RR, 1.36; 95% CI, 1.17–1.58).[32] It was found that 3.6% of those given 600 mg misoprostol had a blood loss greater than 500 mL compared to 2.6% of those given oxytocin.[32] These results can be interpreted as meaning that, for every 100 women given misoprostol instead of oxytocin, one of them will experience blood loss greater than 1000 mL. Again, however, there was no difference in clinically relevant outcomes such as need for transfusion.[32]

Community-Based Studies of Misoprostol for Prevention of Postpartum Hemorrhage

Two RCTs of community-based use of misoprostol for prevention of postpartum hemorrhage are now in progress. In the Gambia, Walraven[34,35] and colleagues are conducting a double-blind randomized study of 1200 women to determine which preparation, 2 mg ergometrine or 600 mcg misoprostol given orally, will be more effective at preventing postpartum hemorrhage (>500 mL), severe postpartum hemorrhage (>1000 mL), and postpartum anemia (<9 g/dL). Trained birth attendants are using the protocol in home births in rural areas. Results are expected in the fall of 2004. The India Site of the Global Network for Women's and Children's research, Belgaum, India, is conducting a double-blind placebo study of 600 mcg misoprostol given orally, administered at home births by trained auxiliary midwives.[36,37] Data collection is ongoing in this study. The midwives are using a specially designed blood collection drape, the BRASS-V Drape[38] to measure actual volume of blood lost after the cord is cut.

The Maternal and Newborn Health Program, a USAID-funded project of the JHPIEGO Corporation, in collaboration with the Ministry of Health of Indonesia and the Ob-Gyn Society of Indonesia, conducted a field demonstration project in two areas of Java, Bandung (intervention site) and Subang (control site).[39] The study was developed to demonstrate that antenatal, community-based distribution of misoprostol and the subsequent self-administration of the drug immediately after home birth could lower the incidence of postpartum hemorrhage among women living in areas where skilled providers do not attend a high proportion of births. Specially trained community health workers using pretested information and counseling materials distributed the misoprostol (three 200-mg tablets for oral use) to women in the eighth month of pregnancy. Women and their families were asked to keep the medication in a safe place with all their home birth supplies. In the intervention area, 93.7% of 1282 women used a uterotonic

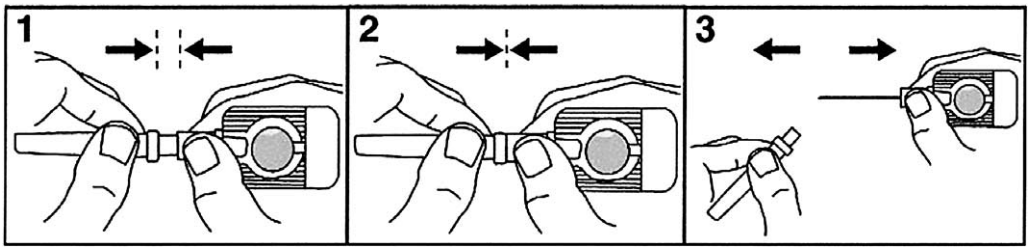

Figure 1. How to "Arm" Uniject. Figure courtesy of Program for Appropriate Technology in Health.

(either injection by the midwife or self-administration of misoprostol) after delivery compared to 76.8% of 475 women in the control area (injection of oxytocin by the midwife only). Nearly 4% of women in the comparison area were referred for postpartum hemorrhage compared to only 2.1% of women in the intervention area. The authors used statistical models in the data analysis to conclude that women in the intervention area were 25% less likely to perceive excessive bleeding, 30% less likely to need an emergency referral to a health facility, and 45% less likely to need an emergency referral for postpartum hemorrhage.[39]

Oxytocin in Uniject

As previously noted, guidelines for the active management of third-stage labor recommend oxytocin, given IM or IV, as the "preferred" uterotonic for prevention of postpartum hemorrhage. However, in many low-resource settings, safe injection is not always possible due to the need for injection skills and training, lack of sterile equipment, and difficulty measuring the correct dose. To overcome some of these barriers to safe injection, the Program for Appropriate Technology in Health (PATH) developed the Uniject device. The device comes individually in a sterile packet and is a prefilled, non-refillable, sterile, easy to use device with a fixed needle that can be "activated" for use after opening the sterile packet (see Figures 1 and 2). The Uniject has been used to deliver tetanus toxoid to pregnant women in Bolivia, Indonesia, and Mali[40–42] and to deliver Cyclofem (a monthly injectable contraceptive containing a combination of the progestin, medroxyprogesterone acetate 25 mg, and the estrogen, estradiol cypionate, 5 mg[43]) to women in Brazil.[44] Studies were conducted on its use to administer oxytocin in Indonesia and in Angola.[45,46] In Indonesia, the study was designed to see 1) if Uniject could be safely used in home settings by skilled attendants (trained village midwives), 2) if the technology of the Uniject improved the delivery of oxytocin, and 3) if it was acceptable to providers and women. The study compared the experiences of 140 midwives who attended 2200 home births using prophylactic oxytocin in Uniject with the midwives' previous experiences with oxytocin in standard syringes. The authors found that unsafe reuse of syringes (previously reported by approximately 33% of the village midwives) ceased once the midwives were supplied with Uniject, that dosage accuracy increased slightly, that mothers found the Uniject less painful than regular syringe injections, and that 98% of midwives preferred the Uniject. Midwives stated that they were willing to pay a small additional amount (over standard syringes) for the convenience of using the Uniject.[45,47]

Possible situations where Uniject could be helpful would be for routine prophylactic use in deliveries by skilled attendants, with improved injection safety, dose accuracy and convenience, selected or emergency use by specially trained providers at community level to prevent or treat postpartum hemorrhage, and/or outreach for use in areas with high rates of postpartum hemorrhage or difficult access to referral care. Other auto-disable syringes are also on the market or coming soon that may help make routine use of injectable oxytoxics safer in low-resource settings.

TREATMENT OF SEVERE POSTPARTUM HEMORRHAGE

Even with major advances in prevention of postpartum hemorrhage, approximately 3% of all women in a variety of populations[21,23,33] will have severe postpartum hemorrhage with blood loss of 1000 mL or more. Those women will require management with stabilization of shock, blood and fluid replacement, and hemostasis of the source of bleeding. Misoprostol for the treatment of postpartum hemorrhage

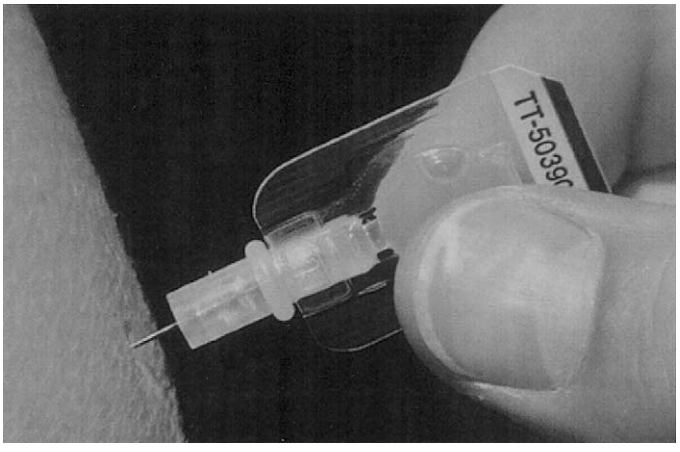

Figure 2. Use of Uniject. Photo courtesy of Program for Appropriate Technology in Health.

and two new technologies for management of severe postpartum hemorrhage are discussed below.

Misoprostol for Treatment of Postpartum Hemorrhage

A recent study from South Africa compared a combination of intramuscular syntometrine injection and oxytocin infusion to rectal misoprostol and found that those who received misoprostol had a statistically significant reduction in bleeding and further medical cointerventions to control the bleeding (6% versus 34%) (RR, 0.18; 95% CI, 0.04–0.67).[48] Sharma and El-Refaey[49] reviewed the South African study and other descriptive, observational, and randomized studies of 800 and 1000 mcg of rectal misoprostol in the treatment of postpartum hemorrhage. They concluded that the use of rectal misoprostol is a relatively easy, non-invasive, and potent treatment for postpartum hemorrhage and recommended that it be added to oxytocin and ergometrine as a first-line agent in the "therapeutic drill" in the steps taken to treat postpartum hemorrhage. They call for further research into the role of misoprostol in the management and treatment of postpartum hemorrhage. A recent Cochrane review also concluded that 800 mcg of rectal misoprostol could be a useful "first-line" drug for the treatment of severe postpartum hemorrhage.[50]

Community-based treatment studies are now under way in Tanzania, Nigeria, and soon to start in Ethiopia and Bangladesh, conducted by the Venture Strategies for Health and Development group with technical assistance from the Bixby Program, School of Public Health, University of California, Berkeley (personal communication, Martha Campbell and Ndola Prata). The Tanzania study, set in rural villages at home births, examines the use of 1000 mcg of misoprostol administered rectally by traditional birth attendants when blood loss is greater than 500 mL.

Antishock Garment

The non-inflatable antishock garment (NI-ASG) is a neoprene garment, much like the bottom half of a wet suit, designed in horizontal segments. Using the elasticity of the neoprene and Velcro fasteners, the garment can apply 30 to 50 mm Hg of pressure to the lower body pressure (Figures 3 and 4). The NI-ASG is a refinement of the pneumatic military (or medical) antishock trousers. Both devices provide circumferential counterpressure to the lower body as a means of resuscitation from hypovolemic shock and hemostasis for bleeding in the lower body. The medical applications of the military antishock garment are described in previous reviews.[51–54]

Compared with the military antishock garment, the NI-ASG is simpler in design, more quickly and easily applied, costs less, and avoids the risk of overinflation and excessive pressure.[55] A single provider can rapidly place a bleeding woman in the garment, and the counterpressure of the NI-ASG will cause a transfer of blood from the lower body and abdomen to the central circulation (brain, heart, lungs, and kidneys). It also provides tamponade to bleeding sites below the level of the diaphragm and diminishes further hemorrhage. In a demonstration project, the NI-ASG has been used for women with postpartum hemorrhage at the Memorial Christian Hospital in Sialkot, Pakistan.[56,57] This obstetric service has a delivery rate of about 8500 annually. In 3 years, more that 150 women were managed with the NI-ASG garment. As in many other developing country contexts, there is no blood bank in the facility (or even in the city); therefore, women with postpartum hemorrhage often have to be stabilized for many hours awaiting blood transfusion and/or surgical management.

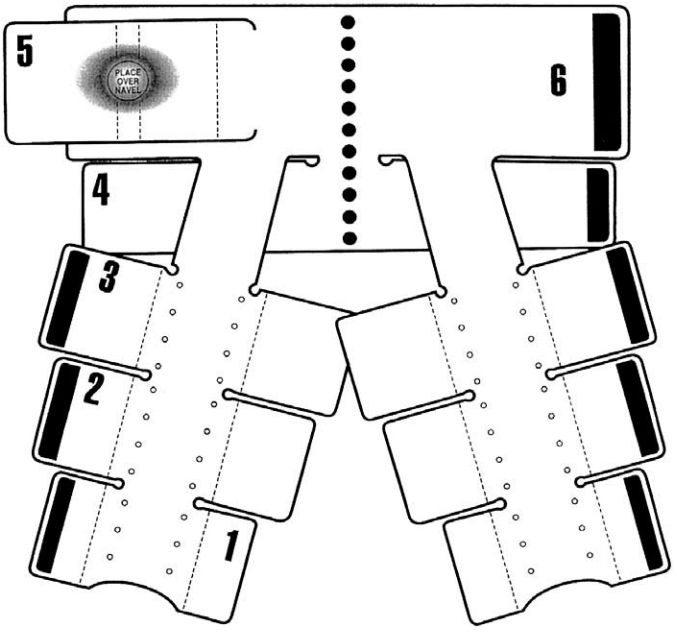

Figure 3. Schematic of non-inflatable antishock garment. Reproduced with permission of the Royal College of Obstetricians and Gynaecologists. From Hensleigh P, 2002.[56]

The outcomes of 21 patients managed with the NI-ASG antishock garment have been reported.[56,57] These reported experiences with the NI-ASG document rapid resuscitation from hypovolemic shock and an extended period of stabilization for patients awaiting blood transfusion and/or surgical intervention. In a combined analysis of the two reports, there appeared to be no adverse effects of prolonging this stabilization period, even though the average interval from diagnosis of hemorrhage to blood transfusion was 5.5 hours and the mean time in the NI-ASG was more than 30 hours.

Women treated with the NI-ASG require nursing care and monitoring of vital signs as any patient with severe hemorrhage and shock does. Placement of a Foley catheter is recommended for continuous monitoring of urine output and, given the design of the device, complete perineal access is possible enabling catheter placement. Likewise, exploration of the genital tract for lacerations, hematoma,

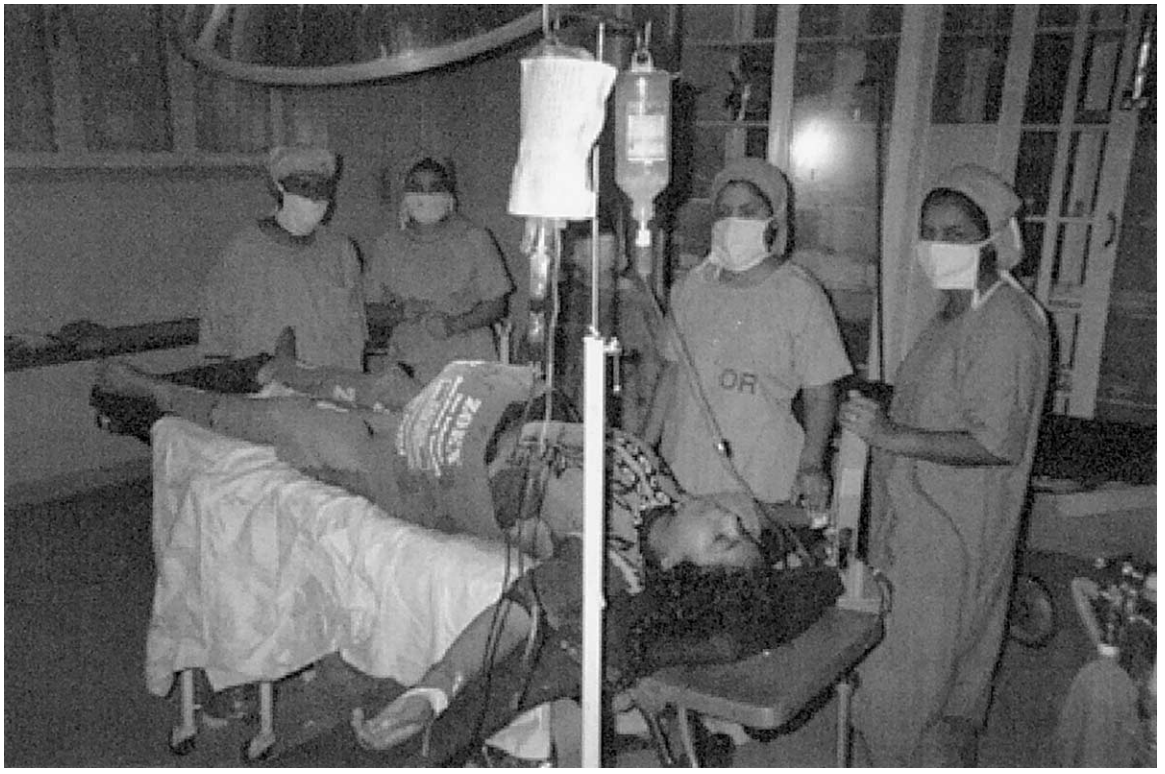

Figure 4. Non-inflatable antishock garment in use. Photo courtesy of Paul Hensleigh.

and other traumatic sources of postpartum hemorrhage is easily accomplished with the NI-ASG in place. Any surgical procedures needed to ensure hemostasis should be completed prior to removal of the NI-ASG. Several of the reported cases involved both preoperative and postoperative use of the NI-ASG with removal of the abdominal portion during the operation. Contraindications to use of the NI-ASG are heart failure, stenotic heart valves, pulmonary edema, bleeding above the diaphragm, and the presence of a viable fetus.

Based on the successes of the small demonstration project in Pakistan, two of the authors, Miller and Hensleigh, will conduct studies using the NI-ASG in similar tertiary care settings in Nigeria and Egypt[58,59] and in rural primary health care facilities with long transport times in Mexico.[58]

Hydrostatic Balloon Condom Catheter

In high-resource settings, the Sengstaken-Blakemore tube[60] and the Rusch urologic hydrostatic balloon catheter[61] have been used to control hemorrhage unresponsive to uterotonics. Both work by creating pressure within the uterus to stop bleeding. However, they are both expensive and not available in many low-resource countries. The hydrostatic condom catheter[62,63] is a sterile rubber catheter fitted with a condom, placed into the uterus through the vagina, and inflated with 250 to 500 mL of saline (Figure 5). To keep the catheter in place, the vagina (not the uterus) must be packed with gauze.

In an observational study conducted in Dhaka, Bangladesh, in 2001 to 2002,[62] 23 women with postpartum hemorrhage due to uterine atony with uncontrolled bleeding following administration of uterotonics had the condom catheter placed. Bleeding stopped within 15 minutes, and no further intervention or treatment was necessary. Oxytocin was administered via IV infusion for a minimum of 6

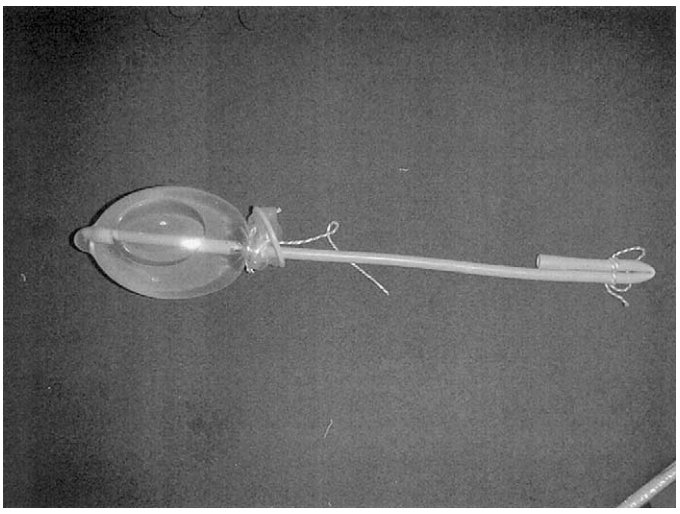

Figure 5. Balloon condom catheter. Photo courtesy of Suellen Miller.

hours after condom catheter placement. The catheter was removed after 24 to 48 hours, depending on the initial volume of blood loss. The condom catheter appeared to effectively control intractable uterine hemorrhage inexpensively and relatively quickly; it can be used by health care providers without access to blood or surgery. Even if surgery and blood transfusions would eventually be required, the use of the condom catheter may, like the NI-ASG, buy time for transport to a facility where definitive therapy would be available. More research will need to be done to determine the efficacy, effectiveness, and risks of the device, but based on this small, observational study, it appears to be a method worth further investigation.

CONCLUSIONS

Enough evidence has been presented in multiple studies to warrant use of active management of third-stage labor; however, because active management of third-stage labor is a multiple-step intervention, further research should be conducted to determine which aspects give the most protection against postpartum hemorrhage and which might hold some risk if used incorrectly or alone. Evidence also supports the use of IM oxytocin injection when conditions are favorable for safe injection. When they are not, the use of the Uniject or oral or rectal misoprostol seems promising. Although the randomized trials at the facility level indicate that oral misoprostol for prevention and rectal misoprostol for treatment are adequately evidence based, it is important to await the results of in-progress community-based studies before recommending widespread use of these medications at the community level.[64] Further research needs to be conducted with both the NI-ASG and the balloon condom catheter. Clinical studies, including either quasi-experimental or randomized cluster design might be conducted as a way to ethically examine their efficacy in developing country settings. One study design would be to test them against one another in a randomized cluster trial with a crossover at midpoint in the study. Given that the NI-ASG, although providing external circumferential counterpressure, also allows perineal access to place the condom catheter to provide intrauterine pressure, both could also be tested together in locations where surgery is delayed.

Postpartum hemorrhage remains the number one killer of women in developing countries. Although there are breakthroughs in the prevention and management of postpartum hemorrhage in high-resource settings, currently access to well-stocked and well-staffed facilities capable of rapid response to the critical emergency of postpartum hemorrhage are lacking in lower-resource settings. The newer technologies and strategies described in this article are promising interventions that may be lifesavers in developing countries. They require further clinical and operations research to demonstrate their effectiveness, efficacy, acceptability, and cost-effectiveness/sustainability before they can be introduced as large-scale programs.

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