

Prevention of Postpartum Hemorrhage: Drug Management Issues in the Active Management of the Third Stage of Labor

1 September 2004



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U.S. Agency for International Development

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This document was made possible through support provided by the U.S. Agency for International Development, under the terms of Cooperative Agreement Number HRN-A-00-00-00016-00. The opinions expressed herein are those of the authors and do not necessarily reflect the views of the U.S. Agency for International Development.

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RPM Plus works in more than 20 developing countries to provide technical assistance to strengthen drug and health commodity management systems. The program offers technical guidance and assists in strategy development and program implementation both in improving the availability of health commodities—pharmaceuticals, vaccines, supplies, and basic medical equipment—of assured quality for maternal and child health, HIV/AIDS, infectious diseases, and family planning and in promoting the appropriate use of health commodities in the public and private sectors.

Recommended Citation

Rational Pharmaceutical Management (RPM) Plus Program. 2004. *Prevention of Postpartum Hemorrhage: Drug Management Issues in the Active Management of the Third Stage of Labor*. Submitted to the U.S. Agency for International Development by RPM Plus. Arlington, VA: Management Sciences for Health.

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PREVENTION OF POSTPARTUM HEMORRHAGE THROUGH THE ACTIVE MANAGEMENT OF THE THIRD STAGE OF LABOR

Uterotonic drugs are used for both the prevention of postpartum hemorrhage (PPH) and the treatment of hemorrhage; however, the Active Management of the Third Stage of Labor (AMTSL) prevention intervention greatly reduces the need for additional drugs and expensive, frequently unavailable, and sometimes risky-to-transfuse blood products used to manage hemorrhage. The prevention focus thus saves lives, valuable financial resources, and time that health care workers must spend providing crisis health care.

Uterotonic Drug Management Issues

To deliver AMTSL effectively, uterotonic drugs, preferably oxytocin, must be on hand to give to the mother immediately after her baby is born. Some uterotonics (e.g., oxytocin, ergometrine, and syntometrine) are heat-sensitive, light-sensitive, or both, and it is essential that they be managed appropriately, so that quality and stability are protected until the drugs are administered. In order to maintain proper temperatures, a “cold chain” must be in place to manage heat-sensitive drugs.

A cold chain is a system of refrigerators, cold boxes, and other devices such as cold packs that maintain the proper temperature for drugs from the point of manufacture to the point of administration.¹ In addition, a system for monitoring temperatures at points along the cold chain (e.g., in refrigerators and freezers) should be operational. Many program planners and managers are already familiar with the concept of the cold chain, which is vital to the storage and distribution of vaccines.

Misoprostol, which does not require cold chain management, is a prostaglandin E1 analogue. It is available in a tablet to be administered orally (i.e., sublingually) and can be stored at room temperature in a closed container. Although this drug has been on the market since 1985 under the brand name Cytotec[®] for the treatment of gastric ulcer, the company that held the patent never applied for approval to use it for obstetric purposes. There are other brand names coming on the market, such as Gynmiso[®] and misoprostol tablets from IVAX, broadening access for use of the drug in obstetric settings.² The U.S. Pharmacopeia has declared PPH prevention to be an “accepted off-label use” for misoprostol.³

¹ Management Sciences for Health and World Health Organization. 1997. *Managing Drug Supply*. 2nd ed. West Hartford, CT: Kumarian Press.

² Association of Obstetrics and Gynecologists of Uganda, Kampala. 2002. “Treatment Guidelines for Misoprostol in Obstetrics and Gynecology.” <www.misoprostol.org> (accessed September 16, 2003).

³ U.S. Pharmacopeia. 2001. *Misoprostol for Prevention of Postpartum Hemorrhage: An Evidence-Based Review by U.S. Pharmacopeia (USP)*. Rockville, MD:USP. <<http://www.uspdqi.org/pubs/other/MisoprostolPoster.pdf>> (accessed Sep. 22, 2003).

Effective Drug Management for Postpartum Hemorrhage

Even well-trained service providers will not be able to provide quality care unless the availability of stable and effective uterotonics is assured. Effective management of uterotonics requires that attention be paid to product selection, procurement, storage, distribution, and use, supported by a policy and regulatory environment that promotes the widespread provision of high-quality drugs.

Program planners need to consider the following four key aspects of pharmaceutical management issues.

Selection

It is critical that program managers choose the right uterotonic for a program, one that is appropriate for the available conditions. (See Table 1.) For example, selection may be guided by the capacity of the supply system to maintain drug quality; drugs requiring a cold chain should only be put into systems that can maintain a cold chain to safeguard effectiveness. Questions to consider—

- What are the drug management storage conditions recommended to protect product quality?
- Are the identified products registered for use in the given setting?
- Are standard treatment guidelines in place for the drug(s) chosen?
- Are skilled providers charged with delivering AMTSL empowered to administer the drug(s) of choice, and do they have the skills to properly perform injections and/or monitor side effects?
- Should more than one type of uterotonic be available in the system?

Procurement

Quantification is the first step in procurement. A careful analysis of the number of facilities, deliveries, and rates of program expansion should be made to estimate the quantity of drugs to be supplied. Because uterotonics are used for other therapeutic purposes, need must be reasonably estimated given the available information. Once quantification is completed, procurement specifications must be set. Questions to consider—

- What quantity of drugs must be available for program use?
- How much of the drug can a program afford to buy initially?
- Are management information systems in place so that consumption patterns can be monitored?

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- Does the program have the capacity to do a forward-looking quantification rather than one based on historical consumption?
- How are medicines currently procured, and will the procurement process and specifications need to be modified?
- Do procurement specifications include criteria to ensure product quality?
- Is the supplier willing to ensure that clear and understandable information on prescribing, administration, and storage is included with the product?
- Can the supplier guarantee a reasonable amount of product shelf life remaining when the drugs are delivered?
- Is there a way to monitor supplier performance?

Storage and Distribution

Most uterotonics require that a cold chain be maintained up to the time of use; therefore, the maintenance of a cold chain is an essential part of a product quality assurance system. Vials or ampoules should not be removed from refrigeration and left on trays for indefinite periods in anticipation of need. Short, monitored periods of time at ambient temperatures seem not to have an adverse affect on oxytocin potency. Issues to consider—

- Is there adequate cold chain equipment in those facilities in which drugs will be either stored or provided? Do facilities have the means to monitor the cold chain (e.g., thermometers and temperature charts)?
- Can the cold chain be maintained during transportation?
- Are pharmacy and storekeeping staff trained in the proper means of storing and dispensing the drugs?
- What are the storage conditions at the health facility level?
- Do providers have a means of accessing refrigerated supplies 24 hours a day?
- For births that take place outside of health facilities, does the birth attendant have a means to safeguard drug quality?
- Are there routine mechanisms to check the product for quality?
- Are records kept on the length of time that drugs are kept out of the cold chain?

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- Would it be better to use a product that is not heat-sensitive, while strengthening the cold chain, so that these uterotonics can be introduced to the program later?
- Are expired drugs removed from the system?

Use

In order for AMTSL to be successful, uterotonics must be used properly. Issues to consider—

- Have all providers been trained in the appropriate use of the uterotonics to be used in the program?
- Is it feasible to train all personnel rapidly?
- Who will train them?
- Are the staff aware of side effects or special considerations for administration?
- Can they counsel and educate patients effectively about the drug, including the purpose, timing of administration, and potential side effects?

IMPLEMENTING AN ACTIVE MANAGEMENT FOR THE THIRD STAGE OF LABOR INTERVENTION

Technical assistance in drug management may be a component of any AMSTL intervention. Targeted assistance can draw upon lessons from other programs and help policy makers and health care administrators identify and address drug management issues related to providing quality PPH prevention services. Infrastructural improvements and personnel training take time and money. A feasibility assessment can determine the best approach for implementing AMSTL. The approach will depend on the skills of providers, the infrastructure, the policy that guides the purchase, the importation of drugs, and any financial constraints.

AMSTL can be introduced using a phased approach, in which a few sites are selected and brought up to standard before others are added, according to a set plan. Or the intervention can be introduced simultaneously to all appropriate sites. The choice of phased versus simultaneous introduction depends on the considerations discussed above. A proactive approach to the management of drug supply will help a program deliver quality services to prevent postpartum hemorrhage.

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Table 1. Considerations in Selection of a Uterotonic

Uterotonic	Storage Requirements	Advantages/Disadvantages
Oxytocin (IM injection)	<ul style="list-style-type: none"> • Store between 15 and 30°C (59 and 86°F) • Protect from freezing 	<ul style="list-style-type: none"> • Effective in 2–3 minutes after injection • Minimal side effects • Can be used in all women • Reduces length of third stage of labor • Inexpensive • Requires cold chain handling and storage
Ergometrine (IM injection)	<ul style="list-style-type: none"> • Store between 2 and 8°C (36 and 46°F) • Protect from light and freezing 	<ul style="list-style-type: none"> • Inexpensive • Effects last 2–4 hours • Contraindicated in women with pre-eclampsia, eclampsia, or high blood pressure • Takes 6–7 minutes to take effect • Can cause nausea and vomiting • Requires demanding handling and storage conditions
Syntometrine (IM injection)	<ul style="list-style-type: none"> • Store between 2 and 8°C (36 and 46°F) • Delivery room stock may be kept at room temperature (but periods of more than 60 days at room temperature prior to use are not recommended) • Protect from light and freezing 	<ul style="list-style-type: none"> • Combined effect of rapid action of oxytocin and sustained action of ergometrine • Relatively more expensive than oxytocin misoprostol much less expensive than prostaglandins • Contraindicated in women with pre-eclampsia, eclampsia, or high blood pressure • Can cause nausea and vomiting • Requires demanding handling and storage conditions
Prostaglandins (IM injection)	<ul style="list-style-type: none"> • Store between 2 and 8°C (36 and 46°F) 	<ul style="list-style-type: none"> • Can be used if first-line oxytocics are ineffective • Much more expensive than oxytocin • Significant side effects include diarrhea, vomiting, and abdominal pain • Contraindicated in women with active cardiac, pulmonary, renal, or hepatic disease
Misoprostol (oral tablet)	<ul style="list-style-type: none"> • Store at room temperature in a closed container 	<ul style="list-style-type: none"> • Easy-to-administer tablet • Does not require cold chain storage • Can be used at home without a birth attendant • Inexpensive • Common side effects are shivering and elevated body temperature