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SPECIAL EDITORIAL

Misoprostol: An essential medicine for managing postpartum hemorrhage in low-resource settings?



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Professor Hamid Rushwan is the Chief Executive of the International Federation of Gynecology and Obstetrics (FIGO). He is a Senior Professor and Consultant in obstetrics and gynecology with over 30 years of experience. Professor Rushwan has a wide range of international expertise and has been actively involved in the field of women's health for the past 2 decades, including clinical work, health services management, research, and teaching. Professor Rushwan has been closely involved in women's health program management and resource allocation activities at a national and international level, and has contributed to the implementation of many successful projects and the establishment of sustainable women's health institutions. Internationally, he has worked as a Senior Professional International Civil Servant at the World Health Organization (WHO) and the United Nations Population Fund (UNFPA). Based in London, Professor Rushwan originally comes from Sudan.

Every day, approximately 1000 women die from preventable causes related to pregnancy and childbirth; 99% of these deaths occur in low-resource countries, with more than half occurring in Sub-

Saharan Africa and one-third occurring in South Asia. These key statistics, taken from a 2010 WHO Fact Sheet on maternal mortality [1], make for stark reading and provide a salutary reminder of the uphill struggle faced by many lower-resource countries as they attempt to reduce levels of maternal mortality and to improve the health outcomes of women and newborns.

Indicators that help to track progress in meeting the goals of the International Conference on Population and Development and the Millennium Development Goals are captured annually in UNFPA's State of World Population report [2], which highlights the disparities between high- and low-resource regions worldwide in terms of, for example, reproductive health, education, and mortality. The latest recorded maternal mortality ratio (maternal deaths per 100 000 live births) in Cameroon, for example, is 1000—compared with 3 in Sweden. In high-resource regions, there is easy access to skilled care at birth; by contrast, a high percentage of women in low-resource countries deliver at home or outside a health facility without immediate recourse to emergency obstetric care or a skilled birth attendant, thus making women more vulnerable to death and disability when complications related to childbirth occur.

One of these complications, severe postpartum hemorrhage (PPH), is widely acknowledged as the leading single direct cause of maternal mortality and morbidity. Alone, PPH accounts for approximately 25% of maternal deaths worldwide, most often affecting the more marginalized, poorest, and underserved women such as those living in remote rural areas of Sub-Saharan Africa and South Asia. Uterine atony, or failure of the uterus to contract after delivery, is the most common cause.

FIGO endorses international recommendations that emphasize the provision of skilled birth attendants and improved obstetric services as central to efforts to reduce maternal and neonatal mortality: an endorsement shared by the International Confederation of Midwives (ICM) in a joint statement [3] and reiterated in a 2011 statement [4] by FIGO. The latter statement provides a comprehensive set of guidelines on best practice for PPH prevention and treatment in low-resource settings. FIGO advocates the use of the 3 components of active management of the third stage of labor, which includes the administration of a uterotonic, by a trained birth attendant to reduce the incidence of PPH.

For optimum use in the prevention and/or treatment of PPH, oxytocin (the gold-standard uterotonic) requires refrigeration, intravenous or intramuscular infusion, and trained providers—factors that can hinder its use in low-resource settings. In settings in which injectable uterotonics are neither available nor feasible, misoprostol (a synthetic E₁ prostaglandin analog) has increasingly been adopted as an alternative intervention strategy—one endorsed by FIGO. The drug is available in tablet form, is relatively inexpensive, and is stable at room temperature.

Until recently, there has been insufficient clinical evidence to lend full support to recommendations for the widespread use of misoprostol for PPH prevention and treatment indications in low-resource settings. Eminent research bodies worldwide have recently begun to fill evidence gaps regarding the safety and efficacy of misoprostol for PPH. The findings from the most recent large-scale clinical studies indicate that the time is ripe for renewed discussions within professional obstetric and gynecologic groups and associations reviewing previous regimen suggestions and recommendations, and for national clinical practices to reflect the current best evidence.

In a randomized controlled trial comparing misoprostol with placebo in a homebirth setting in rural Pakistan [5], 600- μ g oral misoprostol reduced the rate of postpartum bleeding (>500 mL) by 24% when administered by trained traditional birth attendants. The findings from the study corroborate those from seminal studies on misoprostol care at the community level in India [6] and indicate that training and skill building for traditional birth attendants, together with monitoring and evaluation of program effectiveness, should accompany the widespread introduction of misoprostol.

Furthermore, the findings from 2 randomized controlled trials [7,8] undertaken in hospitals in Burkina Faso, Ecuador, Egypt, Turkey, and Vietnam provide evidence of the safety and efficacy of 800- μ g sublingual misoprostol for the treatment of primary PPH. The placebo-controlled trials compared misoprostol with oxytocin. The misoprostol regimen stopped bleeding within 20 minutes of administration in 90% of women. Transient fever and shivering were significantly more likely in women treated with misoprostol but were easily managed by providers, including nurses. The data from these trials indicate that sublingual misoprostol (800 μ g) might be a suitable first-line treatment alternative to intravenous oxytocin for PPH due to uterine atony.

The growing body of clinical evidence has been paving the way for research into the most effective and sustainable service delivery models that meet the needs of women in low-resource and community-based settings, as well as the budgets of cash-strapped countries. An operations research study [9] in the Banke district of Nepal, for example, concluded that community-based distribution of misoprostol, given to pregnant women to self-administer as a prophylaxis, could be successfully implemented under government health services in a low-resource and geographically challenging setting. The proportion of vaginal deliveries protected by a uterotonic, which was the primary measure of performance, rose from 11.6% to 74.2%, with the poor, the illiterate, and those living in remote areas experiencing the most gains. A national roll-out program has now begun in Nepal. A similar study [10] conducted in rural Afghanistan revealed that the 1421 women, including 20 women with twin pregnancies, in the intervention group correctly took misoprostol; the authors concluded that community-based education and distribution of misoprostol for PPH prevention are safe, acceptable, feasible, and effective. They recommended that consideration be given to adopting this strategy in other countries in which access to skilled attendance is limited.

The 18th Expert Committee on the Selection and Use of Essential Medicines took an important step when it approved the addition of misoprostol for the prevention of PPH to the WHO Model List of Essential Medicines. In its unedited report [11]—which was made public in May 2011 following a review of the efficacy, safety, and cost-effectiveness of this and other medicines—the Committee took the decision to move misoprostol from the Complementary to the Core List and to amend the list to include “...and for the prevention of postpartum hemorrhage where oxytocin is not available or cannot be safely used.” The Committee noted that there is “some evidence that 600 mcg given orally is effective and safe” and that new evidence submitted showed that “misoprostol can be safely administered to women to prevent postpartum haemorrhage by traditional birth attendants or assistants trained to use the products at home deliveries.” The Committee further noted that, although misoprostol was not added to the list for its treatment indication, current WHO guidelines [12] recommend the use

of misoprostol for prevention and treatment indications in settings in which it is not possible to use oxytocin or another injectable uterotonic.

FIGO is dedicated to the improvement of women's health and rights, the reduction of disparities in health care available to women and newborns, and the advancement of the science and practice of obstetrics and gynecology. It has, therefore, joined forces with a host of leading agencies involved in safe motherhood initiatives to collaborate on a major project, funded by the Bill & Melinda Gates Foundation and led by Gynuity Health Projects, to address a range of scientific, operational, and policy questions regarding the use of misoprostol for PPH care, thereby empowering providers and health policymakers to arrive at evidence-based decisions that benefit women.

FIGO will pursue its objectives through advocacy, the dissemination of information through diverse media on strong evidence-based results, and the development of materials that will feature on FIGO's website (www.figo.org). Working closely with the FIGO Committee for Safe Motherhood and Newborn Health, professional associations, and other like-minded organizations, the project's activities will include conducting expert panel sessions at regional meetings of obstetricians and gynecologists to highlight the findings of evidence-based clinical studies and to introduce planned studies that shift the emphasis from clinical research into operational realities; publishing scientific articles in the *International Journal of Gynecology and Obstetrics (IJGO)*; producing an *IJGO* supplement; conducting a half-day session at the 2012 FIGO World Congress in Rome; developing user-friendly education and training materials for professional associations and health personnel; offering assistance in the development of guidelines, protocols, and other materials for professional groups at the national level; and conducting national workshops in support of national activities.

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