Misoprostol: A new addition to Post Abortion Care

Gynuity HEALTH PROJECTS

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Summary and Outcomes of Meeting
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Editors

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On October 20, 2003, a group of researchers, policy makers, and program developers came together to explore the use of misoprostol for Post Abortion Care (PAC). The goals of the meeting were to exchange information about misoprostol for PAC and discuss strategies for bringing misoprostol into current PAC protocols. The meeting included a roundtable discussion on the obstacles affecting access to misoprostol and concluded with a discussion of plans for the future. The following is a brief summary of the discussions at the meeting, highlights from the presentations, and a summary of the plan for moving forward with this promising technology.

Beverly Winikoff, of Gynuity Health Projects, opened the meeting with a summary of why misoprostol is primed and ready for introduction into PAC services. Misoprostol is well-known by researchers and clinicians for a variety of reproductive health indications including the treatment of incomplete abortion; however it is less well-known by program planners. It is available in numerous countries around the world; it is cheap and easy to store, transport, and use. It is now time to start the process of producing guidelines for its use in the field.

Anne Burke, of Johns Hopkins University Medical School, gave a summary of the science of misoprostol, its mode of action, and the published research on misoprostol for treatment of incomplete abortion. In summary, misoprostol has been shown to be safe and effective in clinical trials, but studies have not been consistent with regard to route of administration and dosing. Much of the clinical research has been conducted in settings where several technologies for PAC are available, but misoprostol could also be used for PAC in places where safe surgical services are not available. Furthermore, while the medical effectiveness of misoprostol is clear, the programmatic effectiveness warrants further investigation.

Dose finding studies in Vietnam and Thailand, as presented by Jennifer Blum of the Population Council and Gynuity Health Projects, demonstrated that provider training and confidence in the method have a large effect on efficacy. Providers who have less experience, less training, and a lower comfort level, may be quicker to intervene, resulting in a lower overall success rate. The studies also showed that a single dose of 600 mcg oral misoprostol is as effective as a repeated 600 mcg dose (1200 mcg total) for the treatment of incomplete abortion. The single dose regimen may also increase acceptance as it is less cumbersome and more easily provided. The length of time to the follow-up visit is also an important issue. Longer time to follow-up is associated with higher efficacy, as women have been given ample time to complete the process; however, loss to follow-up is also increased with increasing length of follow-up. Determination of an appropriate length of follow-up will maximize efficacy without being so distant as to discourage women from returning.

Godfrey Alia, of Mulago Hospital, Uganda, reported on a recent study that compared the efficacy of misoprostol to MVA for incomplete abortion. Efficacy was found to be similarly high for both treatments, and misoprostol was very acceptable to both women and providers. The issue of high loss to follow up (LFU) in this setting was discussed, and it was noted that while LFU rates are critical in clinical study settings, they may be less critical at the programmatic level. It is essential that women know when they need to seek follow-up care, but it may not be essential that they always return for follow-up visits after receiving postabortion care treatment. Return rates might be increased by the availability of contraceptive services, for example. Dr. Alia described future plans for scaling up misoprostol PAC programs in Uganda, with an aim of reaching peri-urban and rural parts of

the country. The clinical study was coupled with a broad-based policy and education agenda led by the study team in Uganda to target local decision-makers, such as WHO, hospital authorities, and other ob-gyns.

Joan Healy, of Ipas, presented thoughts on the integration of misoprostol into existing PAC programs. Joan emphasized the importance of introducing misoprostol within the context of safe motherhood. She discussed four main issues that condition the use of misoprostol in PAC programs: 1) the availability of the technology, 2) registration of drug for local use, 3) need for a local distributor of the drug and 4) inclusion of the drug in procurement lists. With regard to policy, she mentioned the need to: 1) integrate misoprostol into standards and guidelines for PAC, 2) develop political will and support, and 3) allocate resources for procurement and infrastructure for delivery of services. In terms of advocacy, Joan stressed the importance of increasing community knowledge and awareness about services and the role of provider/community partnerships. Finally, the importance of training, and implementation of appropriate setting-based service delivery systems were highlighted.

A key issue for the use of misoprostol in reproductive health is its lack of a dedicated label in this case for PAC - "No product, no program." Without registration of misoprostol for reproductive health indications such as treatment of incomplete abortion, it may be difficult to integrate its use into PAC programs. Embedding misoprostol into broader reproductive health programs may help to diffuse political sensitivity to a drug that is a known part of medical abortion regimens. Programmatic questions that merit further exploration include:

- How do research protocols translate into clinical practice/programs?
- Are we posing additional barriers by creating strict guidelines for follow-up?
- How can new technologies be introduced while maintaining quality of care?

Erin Gainer, of HRA Pharma, presented information on the role of the pharmaceutical industry in developing misoprostol for PAC. Ms. Gainer walked the participants through an in-depth look at the costs of manufacturing, packaging and distributing a dedicated misoprostol product and the corresponding potential for profit. The conclusion was that under ordinary circumstances, it is not financially feasible or desirable to market a dedicated misoprostol product for reproductive health indications. Furthermore, it is likely that even if a dedicated product is made available, hospitals that routinely stock Cytotec® will still use it for reproductive health indications due to its lower cost. Despite the unclear financial situation, HRA Pharma has registered GyMiso ,a dedicated misoprostol product for induced abortion following mifepristone, which will be available in France in January 2004. Ms. Gainer felt that the French approval would make it more likely that countries in Francophone Africa would register and market the dedicated product for the limited legal indications in the region. Participants then addressed the issue of public/private partnership as a means of building support for a dedicated misoprostol PAC product. Several possibilities were suggested for how this could best be implemented.

- Pharmaceutical companies may need to donate technologies to begin the cycle of demand
- Pharmaceutical companies may need to view developed countries as the setting where they will make money and less-developed countries as the setting where they will 'break even'

Paul Blumenthal, of Johns Hopkins University, moderated a roundtable discussion addressing obstacles to access to misoprostol.

Providers constitute a significant obstacle to the use of misoprostol in postabortion care. Despite a small, but significant body of evidence in support of misoprostol for this indication, providers are often reluctant to change their current practice. The data required to convince providers may be different from the data needed to convince regulatory agencies of misoprostol's safety and efficacy. For providers, are clinical data sufficient to warrant misoprostol's use? How much data is enough? While providers and policy makers are often convinced by regulatory bodies, the opposite can also be true in that regulatory agencies may take their cues from provider practices. The lack of a standardized dose and regimen creates another problem for providers. However, research has shown that many doses work well and that resources may not be well spent in the search for the "perfect dose." Again, this programmatic and provider perspective may conflict with the needs of regulatory bodies. It was also noted that while a search for the perfect dose may not be reasonable, many regulatory agencies do value promotion of the lowest possible effective dose. Of the many different kinds of research, two were addressed specifically in regard to misoprostol for PAC: research to create a label and research into development of a program. While both kinds of research are important, the full scope of information is not essential for regulatory purposes. And the entire regulatory label is not essential for programmatic purposes.

Another important obstacle to the use of misoprostol for PAC is provider training. Who decides if a woman is eligible for misoprostol? How trained is that decision maker? Should training be aimed at mid-level providers? Will upper level providers resent the loss of income if potential surgical patients receive medical treatment elsewhere? The general feeling is that if the treatment is available and acceptable, over time it will be included in normal practice.

The use of misoprostol in restrictive abortion settings was also discussed. Given the broader policy implications in these settings, it may be necessary to bring policy makers on board before trying to introduce misoprostol for PAC. How do we address the issue of misoprostol's known abortifacient properties when dealing with policy makers? It may be useful to emphasize misoprostol's value for "safe motherhood" generally and stress its broad range of uses in reproductive health. In order to be accepted among policy makers, misoprostol will require the vocal support of safe motherhood organizations. Furthermore, it would help to stress the public health contribution of this drug in that it reduces maternal mortality and morbidity. Since policy makers are interested in saving money on programs, a cost effectiveness or costing study could be pivotal in gaining policy maker interest.

Participants voiced their support for integrating misoprostol into family planning services. This technology takes PAC out of the procedure room, reduces stigmatization, and puts it in closer proximity to family planning. Misoprostol may prove to be a more effective link to family planning than MVA.

The discussion concluded with resounding agreement that the World Health Organization needs to be convinced to put misoprostol on its Essential Drugs List (EDL). A submission requesting this action was previously rejected due to the lack of a registered Ob/Gyn indication for misoprostol. However, there is no mandate that the WHO follow the

decisions made by pharmaceutical companies. WHO works on misoprostol for PPH treatment and as a drug for medical abortion. If research shows the utility of misoprostol for treatment and/or prevention of PPH, this may prove to be a big step in getting the drug on the EDL.

After this roundtable discussion, Sue Griffey moderated a discussion of next steps:

Inputs Needed to Promote Misoprostol for Postabortion Care

- Research to develop a label, demonstration projects, operations research
- Translate research into service delivery
- Create program for implementing service delivery
- Expand PAC programs to save women's lives and re-integrate family planning and position PAC in broader reproductive health context
- Ensuring that providers feel comfortable with program and service delivery strategies
- Increasing knowledge-sharing and awareness-building about misoprostol for PAC
- Decentralizing programs to allow district level decision-making and power-sharing

Goals for misoprostol for PAC

Short term:

- At APHA: PAC consortium meeting should include discussion of how to include use of misoprostol from programmatic perspective
- USAID: Voiced a commitment to emphasize misoprostol for PAC in conversations and meetings
- Knowledge sharing: A listserve will be created to disseminate findings and experiences – specifically from Dr. Alia's research in Uganda

Medium term:

- Identify opportunities within our own projects/organizations for PAC projects
- Hold consensus meeting on instructions for use of misoprostol for PAC sanctioned by core group (need individuals with technical expertise) – will be organized by Gynuity and held in the spring 04
- Produce position document for broad audience on use of misoprostol for PAC (several existing documents were identified that could possibly be edited in order to produce this)
- Produce template for what a demonstration project looks like
- Conduct comparative cost measurement of misoprostol and MVA or D+C
- Include PAC in pre-meeting planning agenda for Cairo +10 in London 2004
- Identify regional leaders in order to facilitate training cascading within a region
- Identify pharmaceutical companies promoting misoprostol for ob-gyn indications
- Identify status of misoprostol in each country and whether governments are willing to make the drug available non-commercially and whether governments are willing to

promote it for PAC. A 3x2 table could serve as a framework, and distinct strategies be developed for each cell.

Status of Misoprostol	Government willing	Government not willing
Approved and marketed for RH indication		
Approved and marketed for GI indication		
Not yet marketed		

Long term:

- Locate funding from international donors for PAC
- Advocate for misoprostol to be on the WHO's essential drug list
- Scale up use and advocacy to provide women with access to treatment in a variety of global settings

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