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Health officers provide information about maternal health in Bangladesh, a country that lets pregnant women have the drug misoprostol.

Access denied

Misoprostol could save the lives of women who give birth at home, but the drug is restricted — in part because it can be used to induce abortions. **By Alla Katsnelson**

As a girl growing up in Angola, Ndola Prata listened to the women of her family voice the seemingly insurmountable problems they faced in trying to control their fertility. They ranged from the struggle to afford reliable contraception to the acute danger of dying in childbirth or from an unsafe abortion. At every turn, it seemed to her, they were mired in the burdens of trying to navigate this central aspect of their lives.

These women's struggles fuelled Prata's drive to become a doctor dedicated to improving women's health. And her resolve grew in the early days of her career when, while working in the main maternity hospital of Luanda, she watched a woman die from postpartum haemorrhage after an apparently normal delivery. "The first one is the one that shocks you," says Prata, now director of the Bixby Center for Population, Health and Sustainability at the University of California, Berkeley.

The woman who died had received the hormone oxytocin, which is the preferred treatment for postpartum haemorrhage, but it didn't work. Perhaps, says Prata, the oxytocin was not refrigerated, as it should be — and Prata had no other treatments to offer.

But during the 1980s, a new option emerged. Misoprostol is a synthetic analogue of a lipid called prostaglandin E1 and had been developed to prevent and treat ulcers. Its label warned against taking it while pregnant because it causes uterine contractions.

As the drug came to pharmacies around the world, physicians and researchers soon started to take notice. They realized that the drug's effects on the uterus meant it could have a host of other uses — such as preventing and treating postpartum haemorrhage, the leading cause of maternal death worldwide. But it was also being used to cause abortions.

Misoprostol answered a clear, unmet need. Oxytocin is administered by injection but it is expensive and is often out of stock at health facilities in low- and middle-income countries (LMICs). Misoprostol, by contrast, is cheap and can be stored at room temperature, making it ideal for LMICs."A lot of us were intoxicated by its potential," says Andrew Weeks, a maternal-health researcher at the University of Liverpool, UK. By the 1990s, researchers were exploring its effects. Many, including Weeks, were testing its efficacy and devising protocols for a hospital setting.

But Prata's vision went further. Her aim was to give women the power to control their own

reproductive health. Many women in LMICs, for various reasons, do not give birth at a medical facility but at home, either alone or with the help of a birth attendant. "We wanted to open people's eyes to an opportunity we never had before," she says. Misoprostol represented "a possibility to do something for people who deliver at home".

The idea of giving women and their birth attendants, who are not medically trained, a drug to administer on their own was radical at the time, particularly because the drug could also be used for abortion. Many people are still opposed to the idea today, says Prata.

Safety first

The World Health Organization ranks misoprostol just below oxytocin on the list of preferred drugs to prevent postpartum haemorrhage, and it is recommended when oxytocin is not available. Yet until November 2020, there was no clear recommendation to support its distribution to pregnant women for self-administration.

More than 20 countries in Asia and Africa have studied approaches to distribute misoprostol to women to prevent postpartum haemorrhage, either through government public-health programmes or through non-governmental organizations, but many countries have stopped short of scaling up these programmes. "Because of its association with abortion, a lot of governments have ended up being very cautious with it," says Weeks.

Over the past two decades, Prata and a small group of maternal-health researchers have demonstrated the value of misoprostol in LMICs outside a hospital setting. "It was kind of threading the needle, walking around the politics," says Beverly Winikoff, a family-health researcher at Columbia University in New York City, who was one of the group's leaders. There has been, she says, a "reluctance to give women the power in their own hands".

Prata thinks that access to misoprostol today is less widespread than it should be. She is adamant that the research clearly shows that the drug safely and effectively prevents postpartum haemorrhage when women are shown how to use it. Its widespread use has contributed to a 35% decline in maternal deaths worldwide between 2000 and 2017.

Women first started using misoprostol to terminate pregnancies in Brazil, after the drug was approved in 1986. The government quickly clamped down on this off-label use because abortion was, and still is, illegal in the country. But the drug remained available on the black market and has dramatically reduced Brazil's soaring rate of hospitalizations caused by botched abortions.

Word spread throughout Latin America and beyond. Cassimo Bique, a gynaecologist at Maputo Central Hospital in Mozambique, began using misoprostol to induce labour around 1992. A colleague who had travelled to Brazil then suggested using it for abortions, which the hospital began to do. Bique and his colleagues were soon also using the drug to prevent and treat postpartum haemorrhage, he says – an idea that spread to other Mozambique hospitals. Meanwhile, Weeks and others began testing the approach at hospitals around the world.

Home help

In the early 2000s, Prata's team was one of the first to roll out pilot studies to test whether misoprostol was safe and effective for preventing postpartum haemorrhages in women who give birth at home with no assistance beyond the birth attendants. These early studies were supported by the US Agency for International Development and other donor organizations.

Her objective was to convince countries to register misoprostol and to set up frameworks to distribute it widely. The results were clear, she says: all the women took the drug correctly, and it reduced the number of acute cases of postpartum haemorrhage by as much as half.

Despite this success, some health officials and researchers balked at attempts to make misoprostol widely accessible to women. The problem, says Weeks, is that in ideal circumstances, oxytocin is more effective than misoprostol in reducing postpartum haemorrhage. So for some researchers, promoting the use of misoprostol over oxytocin amounted to giving poorer women worse treatment than richer ones. Prata and others argued that oxytocin was impractical in many settings and that misoprostol could fill the gap.

Researchers also worried that giving pregnant women the drug to use themselves would undermine efforts to encourage them to give birth more safely in hospital or with trained midwives. But the data did not support this concern. "If anything, it increased the chances that women would come to the hospital," says gynaecologist Jeffrey Smith, deputy director of maternal, newborn and child health at the Bill and Melinda Gates Foundation in Seattle. "This just gave women the alternative, so if they couldn't get to the hospital, there was something they could do to protect their health."

The main concern of some of the naysayers, according to Prata – and one that riles her greatly – is that women and their birth attendants, who are often uneducated and illiterate, would not be able to follow the instructions for using the pills safely. When used incorrectly at the very end of pregnancy, the drug can cause the uterus to rupture. But this fear was also misplaced. "In country after country after country, we basically just demonstrated it was OK," says Prata.

Today, the main barriers to global acceptance and recommendations to use misoprostol for postpartum haemorrhage have been largely overcome. A few countries, including Nepal, Bangladesh, Afghanistan and Mozambique, have strong systems in place to distribute misoprostol to women before they give birth. Still, access in other nations remains patchy – a concern that is especially important during the COVID-19 pandemic, when more women are likely to give birth at home because of a fear of going to the hospital.

Prata is now conducting studies on whether and how women can safely use misoprostol – ideally, in combination with a steroid called mifepristone – in LMICs to terminate early-stage pregnancies. Increasing access to the drug might well lead to more abortions, she says. "But women who want to terminate their pregnancies are not waiting for this drug," she says. "From a public-health perspective, I would actually say: 'Let me tell you how to use it correctly, because this would be safer than any other way you've been thinking of."

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Winikoff thinks that the COVID-19 pandemic might make health officials more open to the idea of using drugs such as misoprostol for self-care. Prata agrees. She hopes to soon launch a study of telemedicine abortion in sub-Saharan Africa. "Now, with COVID-19, where a lot of things have shifted to telemedicine, we are trying to push that agenda forward," she says.

Prata often thinks back to when she told her grandmother, upon graduating from medical school, that she wanted to give women the tools and knowledge to make their own decisions around family planning. "My grandmother said: 'This is very nice, but you have to remember to always put yourself in their shoes'." That, she says, means trusting and empowering women to control their own reproductive health.

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