Commentary

Mifepristone for emergency contraception: Case for recommendation in practice guidelines

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One in four pregnancies is unintended, threatening the lives and well-being of women and adolescents globally [1]. The risks of unintended pregnancy are greatest in low- and middle-income countries where maternal mortality rates are highest [2]. Emergency contraception (EC) is an effective and essential intervention to prevent unintended pregnancies, however barriers at the client, provider, and system levels exist [3,4].

Multiple EC options are currently recommended in global guidelines including combined hormonal contraceptive pills, levonorgestrel (LNG) alone, ulipristal acetate (UPA) and intrauterine device (IUD) insertion [5]. A key obstacle to EC use has been the limited availability of the most effective forms. IUD insertion can be performed only in facilities and applies to women opting for ongoing contraception hence not widely implementable. Studies have demonstrated that UPA offers a significant comparative advantage over LNG, however its cost makes it inaccessible precisely where it is needed most: low and middle income countries [6]. UPA is currently registered in 59 countries. However, UPA is still under patent (until 2030) and there are no preferential pricing arrangements for the public sector of low- and middle-income countries. A public sector price for UPA is urgently needed. In the absence of a change in UPA pricing, women need access to an equally effective and affordable option.

An effective, available, and affordable option for oral EC exists: mifepristone. Mifepristone is a progesterone antagonist with multiple potential applications for use in gynecology. It is widely underutilized for use as EC, despite compelling evidence for its efficacy. The Cochrane review on interventions for emergency contraception includes 115 trials published between 1987 and 2014 [7]. Fifty-six of these trials were dose-comparison studies of mifepristone ranging from 5 to 600 mg, and a further forty-one trials compared LNG with mifepristone. The review provides compelling evidence that both mifepristone at 25–50 mg doses and UPA are more efficacious than LNG with a similar effect size reducing EC failure by approximately 40% compared to LNG. The similarity in effect size is not surprising: both mifepristone and UPA belong to the same class of medications.

Mifepristone is a safe, effective and affordable option for EC, however its availability globally has been limited. Only six countries have a registered mifepristone product for EC and none of those products are quality-assured. Lack of mifepristone availability for EC is in part due to the absence of a global recommendation for its use as EC. While mifepristone is referenced by some organizations as an option for EC, it is not currently recommended by the World Health Organization (WHO) as an option for EC. Inclusion of mifepristone in WHO guidelines on emergency contraceptive use is an important first step to expanding access to effective EC globally. A recommendation from WHO on clinical use would facilitate the inclusion of mifepristone for EC on the WHO Essential Medicines List, which would expedite manufacturing and registration of a dedicated, quality-assured mifepristone EC product in diverse countries. It is unlikely that a manufacturer would create a dedicated mifepristone EC without a global recommendation to facilitate its clinical use and purchase by the public (and private) sector especially in low- and middle-income countries. WHO advanced the care and treatment of millions of people living with HIV/AIDS, by issuing global guidelines on the use of antiretroviral
therapy and making a concurrent recommendation for inclusion on the Essential Medicine list in the early 2000s. Unintended pregnancy is a major contributor to maternal morbidity and mortality worldwide; a global recommendation and inclusion on the WHO Essential Medicines List of mifepristone may similarly improve health globally.

WHO demonstrated leadership and vision in conducting the international trials that demonstrated the efficacy of mifepristone as EC. It is not known why mifepristone has been excluded from current clinical recommendations on EC use, but this may reflect the association of mifepristone with abortion or its limited international availability in mid 2000s. While oral medications for both EC and medical abortion have existed for many years, the discovery of mifepristone as an abortifacient coincided with the wide marketing of dedicated oral agents for EC. Political controversy surrounding medical abortion frequently challenged the use of antiprogestins for EC. It is possible that in the early 2000s mifepristone was excluded from global EC recommendations to minimize confusion regarding the purpose of the products. However, as of 2020, mifepristone is registered in 55 countries either as a single drug or co-packaged with misoprostol for abortion. At least in those countries political sensitivities should not be a concern for bringing a dedicated mifepristone EC product.

It is time to re-evaluate mifepristone’s role in EC and include it in global guidelines for EC use. Mifepristone inclusion in global guidelines for EC is an essential step in the path to making it accessible. Manufacturers can then engage in quality-assured manufacturing of products that are affordable, and register and introduce them in low- and middle-income countries. Once there is a recommendation, the global sexual and reproductive health community can support the necessary processes to make the medications widely available. As long as UPA remains out of reach for many, efforts to expand effective options must be pursued. While concerns about the conflation of emergency contraception and medical abortion continue to present a challenge, fear of controversy is not enough to continue to exclude mifepristone from EC recommendations.

References